```
=> fil reg

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STRUCTURE FILE UPDATES:     3 APR 2001  HIGHEST RN 329897-04-3
DICTIONARY FILE UPDATES:    3 APR 2001  HIGHEST RN 329897-04-3

TSCA INFORMATION NOW CURRENT THROUGH July 8, 2000

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Structure search limits have been increased.  See HELP SLIMIT
for details.

=> d sta que l6

L1                STR
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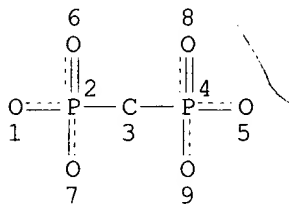

Point of Contact:
Jan Delaval
Librarian-Physical Sciences
CM1 1E01 Tel: 308-4498

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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   9

STEREO ATTRIBUTES: NONE
L3          9837 SEA FILE=REGISTRY SSS FUL L1
L4                STR
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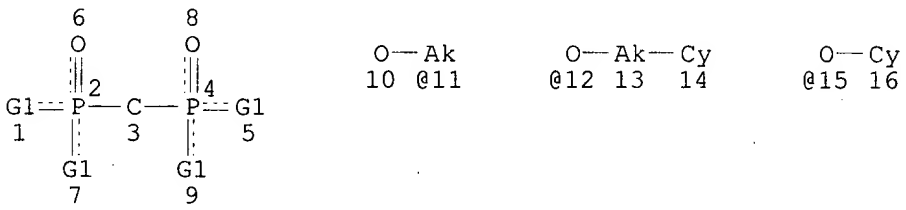


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VAR G1=OH/11/15/12
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE
L6          5983 SEA FILE=REGISTRY SUB=L3 SSS FUL L4

100.0% PROCESSED   9837 ITERATIONS                    5983 ANSWERS
SEARCH TIME: 00.00.10
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=> d his l6-

     (FILE 'REGISTRY' ENTERED AT 09:54:49 ON 04 APR 2001)
L6          5983 S L4 FUL SUB=L3
                 SAV L6 KWOON7199A/A
L7           411 S L6 AND (ADEN? OR GUAN? OR THYM? OR CYTID? OR URAC?)
L8          5572 S L6 NOT L7

     FILE 'HCAPLUS' ENTERED AT 10:07:04 ON 04 APR 2001
L9          6750 S L8
L10          235 S L7

     FILE 'REGISTRY' ENTERED AT 10:07:38 ON 04 APR 2001
L11         3854 S L3 NOT L6-L8

     FILE 'HCAPLUS' ENTERED AT 10:07:51 ON 04 APR 2001
L12         2446 S L11
                 E AUTOIMMUN/CW
L13         5718 S E4,E5
                 E AUTOIMMUN/CT
                 E E9+ALL
L14        12099 S E3,E2+NT
                 E AUTOIMMUNI/CT
                 E E4+ALL
L15          936 S E1,E2
L16          672 S HASHIMOT? (L) THYROID?
L17         1993 S MYASTHEN? (L) GRAV?
L18         6961 S LUPUS (L) ERYTHEMAT?
                 E LUPUS/CT
                 E E9+ALL
L19         5510 S E5,E4+NT
                 E HASHIMOTO/CW
                 E THYROIDITIS/CW
L20          130 S E3
                 E THYROIDITIS/CT
                 E E3+ALL
L21          367 S E2
                 E MYASTHEN/CW
L22         1648 S E4
                 E MYASTHEN/CT
                 E E5+ALL
L23         1648 S E5
                 E DIABETES MELLITUS/CT
                 E E3+ALL
L24        37888 S E4+NT
L25        42636 S  DIABET? (L) MELLIT?
L26        14201 S DIABET? (L) INSULIN (L) DEPEND?
L27         1027 S PRIMARY (L) BILIAR? (L) CIRRHOS?
                 E PRIMARY BILIARY/CT
                 E E4+ALL
L28          406 S E1,E2
                 E CIRRHOSIS/CW
L29          486 S E3 (L) BILIAR?
                 E CIRRHOSIS/CT
                 E E5+ALL
L30          342 S E6,E5
                 E CIRRHOSIS/CT
                 E E3+ALL
L31           42 S E5,E6 (L) BILIAR?
L32        11494 S HEPAT? (L) CHRONIC
                 E HEPATITIS/CW
L33         2496 S E3 (L) CHRONIC
                 E HEPATITIS/CT
                 E EE16+ALL
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                E HEPATITIS/CT
                E E16+ALL
L34          32 S E2
L35         225 S E1
                E HEPATITIS/CT
                E E3+ALL
L36        2385 S E6+NT (L) CHRONIC
L37         655 S E11-E14
L38         537 S ADDISON? (L) (DISEASE OR DISORDER OR SYNDROM?)
                E ADDISON/CT
                E E5+ALL
L39         307 S E5
L40          52 S HYPOADRENOCORT?
L41         431 S POLYMYOSIT? OR POLY MYOSIT?
                E POLYMYOSIT/CW
L42          77 S E4
                E POLYMYOSIT/CT
                E E4+ALL
L43         215 S E2,E1
                E DERMATOMYOSIT/CW
L44         234 S E4
                E DERMATOMYOSIT/CT
                E E4+ALL
L45         234 S E9
L46         345 S DERMATOMYOSIT?
L47         557 S AUTOIMMUN? (L) (ANEMI? OR ANAEMI?)
L48         414 S AUTOIMMUN? (L) (ANEMI? OR ANAEMI?) (L) (HAEMOLYT? OR HEMOLYT?
                E ANEMI/CT
                E E5+ALL
L49         686 S E4 (L) (HEMOLYT? OR HAEMOLYT?)
L50         612 S E3 (L) (HEMOLYT? OR HAEMOLYT?)
L51          94 S E11
L52         710 S E3+NT (L) (HEMOLYT? OR HAEMOLYT?)
L53        1194 S MYOCARDIT?
                E MYOCARDIT?/CW
L54         178 S E4
                E MYOCARDIT?/CT
                E E4+ALL
L55         354 S E2
L56         178 S E1
                E MYOCARDIT?/CT
                E E6+ALL
L57          91 S E1,E2
                E MYOPERICARDIT/CW
L58           2 S MYOPERICARDIT?
                E PERICARDIUM/CW
L59          46 S E3 (L) PERICARDIT?
                E SCLERODERM/CW
L60         306 S E4
                E SCLERODERM/CT
                E E5+ALL
L61         812 S E2
                E SCLERODERM/CT
                E E4+ALL
L62         259 S E1
L63        1608 S SCLERODERM?
                E UVEITIS/CW
L64         155 S E3
                E UVEITIS/CT
                E E3+ALL
L65         475 S E1,E2
                E UVEITIS/CT
                E E4+ALL
L66          62 S E2
L67        1024 S UVEITI?
                E PHACOUVEIT/CW
```

```
L68           0 S PHACOUVEIT?
L69           0 S ?COUVEIT?
                E OPHTALMIA/CW
L70           0 S OPHTALMIA
L71          49 S OPHTHALMIA
                E OPHTHALMIA/CW
L72         310 S PEMPHIG? (L) VULGAR?
                E PEMPHIG/CW
L73           2 S E6,E7 (L) VULGAR?
                E PEMPHIG/CT
                E E10+ALL
L74         114 S E1,E2
                E PEMPHIGUS VULGARIS/CT
                E E4+ALL
L75         579 S PEMPHIGOID
                E PEMPHIGOID/CW
L76          49 S E3
                E PEMPHIGOID/CT
                E E4+ALL
L77         161 S E2
L78         594 S PERNICI? (L) (ANEMI? OR ANAEMI?)
                E ANEMI/CW
L79         307 S E4 (L) PERNIC?
                E ANEMI/CT
                E E5+ALL
L80         307 S E4,E3+NT (L) PERNIC?
L81         726 S ATROPH? (L) GASTRI?
                E ATROPHIC/CT
                E E4+ALL
L82          58 S E2
                E GASTRI/CT
L83          51 S GASTR?/CW (L) ATROPH?
L84         154 S STOMACH?/CW (L) ATROPH?
L85         131 S L84 (L) GASTR?
L86        2435 S CROHN? (L) (DISEASE OR DISORDER OR SYNDROM?)
                E CROHN/CW
L87         526 S E3
                E CROHN/CT
                E E6+ALL
L88         526 S E1,E2
L89        2770 S  (COLIC OR COLIT?)(L)ULCER?
                E COLIT/CW
L90         568 S E4 (L) ULCER?
                E COLIT/CT
                E E4+ALL
L91        1875 S E2,E1
                E ULCER/CT
                E E3+ALL
L92           2 S E3,E2 (L) (COLIT? OR COLIC)
L93       38065 S ALLERG?
L94         545 S HAYFEVER OR HAY FEVER
L95       10105 S POLLEN
                E ALLERG/CW
L96       24554 S E4-E6,E8
                E ALLERG/CT
                E E6+ALL
L97        5804 S E3
                E E7+ALL
L98       15176 S E3,E4,E2+NT
                E E26+ALL
L99         517 S E4
L100      23883 S AUTOIMMUN? OR AUTO IMMUN?
                E IMMUN/CW
L101       1379 S E4,E6 (L) AUTO
L102         59 S L9 AND L13-L101
L103          0 S L10 AND L13-L101
```

```
L104          15 S L11 AND L13-L101
L105          70 SS L102,L104
                 E JOMAA H/AU
L106          26 S E3,E4
L107           2 S L106 AND L13-L101
L108           2 S L106 AND L9,L10,L12
L109           3 S L107,L108
L110        6291 S MULTIP? (L) SCLEROS?
                 E MULTIPLE SCLER/CT
                 E E4+ALL
L111        4389 S E3+NT
                 E SCLERO/CT
                 E E112+ALL
L112        1819 S E2,E1
L113         472 S E1,E2 (L) MULTIPL?
L114           4 S L9,L10,L12 AND L110-L113
L115          70 S L105,L114
L116           1 S L106 AND L110-L113
L117           3 S L109,L116
L118          72 S L115,L117
L119          51 S L115 AND (PD<=19980626 OR PRD<=19980626 OR AD<=19980626 OR PY
L120          36 S L119 AND (1 OR 63 OR 15)/SC
L121          21 S L119 AND (1 OR 63 OR 15)/SX
L122          46 S L120,L121
L123           5 S L119 NOT L122
L124           3 S L123 NOT (8 OR 5)/SC
L125          49 S L122,L124
L126        1104 S L9 (L) THU/RL
L127           6 S L10 (L) THU/RL
L128          87 S L12 (L) THU/RL
L129          29 S L125 AND L126-L128
L130           9 S L129 AND (AUTOIMMUN? OR IMMUNITY OR IMMUNE)/CW
L131           7 S L129 AND (MATRIX OR SH2 OR PACLITAXEL OR COLLAGEN OR TOLERAB?
L132          22 S L129 NOT L131
L133          22 S L130,L132
L134          20 S L125 NOT L127-L133
L135           9 S L134 AND (RHENIUM OR COLLAGENASE OR ENDOTOXIN OR ATP OR BLADD
L136          11 S L134 NOT L135
L137          35 S L117,L133,L136
                 SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 11:02:57 ON 04 APR 2001
L138          62 S E1-E63                          <- hits for L137
                 SAV L138 KWON7199B/A

     FILE 'REGISTRY' ENTERED AT 11:03:49 ON 04 APR 2001

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 11:04:10 ON 04 APR 2001
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FILE COVERS 1967 - 4 Apr 2001  VOL 134 ISS 15
FILE LAST UPDATED: 3 Apr 2001  (20010403/ED)

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=> d l137 all fhitstr tot

L137 ANSWER 1 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:347 HCAPLUS
DN 132:59143
TI Use of bisphosphonates for the prophylaxis and treatment of infectious processes in humans and animals and for herbicides
IN **Jomaa, Hassan**
PA Germany
SO Ger. Offen., 8 pp.
CODEN: GWXXBX
DT Patent
LA German
IC ICM A61K031-66
CC 1-5 (Pharmacology)
Section cross-reference(s): 5
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19859668	A1	19991230	DE 1998-19859668	19981223
	WO 2000038660	A2	20000706	WO 1999-EP10350	19991223
	WO 2000038660	A3	20001221		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI DE 1998-19827986 19980624
DE 1998-19859668 19981223
OS MARPAT 132:59143
AB Bisphosphonates are disclosed for the prophylaxis and treatment of infectious processes in humans and animals which are caused by viruses, bacteria, fungi, or parasites, and as a herbicide for plants.
ST antiinfective herbicide bisphosphonate; bactericide virucide fungicide parasiticide bisphosphonate
IT Trypanosoma cruzi
(Chagas' disease from; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)
IT Cryptosporidium
(Cryptosporidiosis; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)
IT Sarcocystis
(Sarcocystosis; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)
IT Balantidium
(balantidiosis; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)
IT Acanthamoeba
Actinobacillus
Actinomyces
Actinomycetaceae

Adenoviridae
Aeromonas
Aeromonas salmonicida
Alphavirus
Anti-infective agents
Antibacterial agents
Antimalarials
Antiviral agents
Aphthovirus
Arenaviridae
Arenavirus
Aviadenovirus
Avipoxvirus
BK virus
Bartonellaceae
Bordetella
Borrelia
Borrelia burgdorferi
Brucella
Bunyaviridae
Bunyavirus
Caliciviridae
Campylobacter
Campylobacter coli
Campylobacter fetus
Campylobacter jejuni
Capripoxvirus
Chlamydia psittaci
Chlamydia trachomatis
Chlamydiaceae
Clostridium
Coccidiosis
Coronaviridae
Corynebacterium
Corynebacterium diphtheriae
Corynebacterium pseudotuberculosis
Cytomegalovirus
Densovirus
Dependovirus
Dermatophilus
Ebola virus
Enterovirus
Erysipelothrix rhusiopathiae
Filoviridae
Flaviviridae
Flavivirus
Fungicides
Giardia
Giardia lamblia
Hantavirus
Helicobacter
Helicobacter pylori
Hepadnaviridae
Hepatitis A virus
Hepatitis B virus
Hepatitis C virus
Hepatitis E virus
Hepatitis F virus
Hepatitis G virus
Hepatitis delta virus
Hepatitis virus
Herbicides
Herpesviridae
Human T-lymphotropic virus
Human coxsackievirus
Human echovirus

Human herpesvirus
Human herpesvirus 3
Human herpesvirus 4
Human herpesvirus 6
Human herpesvirus 7
Human herpesvirus 8
Human immunodeficiency virus
Human poliovirus
Influenza virus
JC virus
Legionella
Legionellaceae
Lentivirus
Leporipoxvirus
Leptospira
Leptospiraceae
Listeria
Listeria monocytogenes
Listonella anguillarum
Lymphocytic choriomeningitis virus
Lyssavirus
Marburg virus
Mastadenovirus
Measles virus
Miopapovavirus
Molluscum contagiosum virus
Moraxella
Moraxella bovis
Morbillivirus
Mumps virus
Mycobacteriaceae
Mycobacterium avium
Mycoplasma
Mycoplasma pneumoniae
Mycoplasmataceae
Naegleria
Nairovirus
Neisseria
Neisseria gonorrhoeae
Neisseria meningitidis
Neisseriaceae
Nocardia
Orbivirus
Orthomyxoviridae
Orthopoxvirus
Papillomavirus
Papovaviridae
Paramyxoviridae
Paramyxovirus
Parapoxvirus
Parasiticides
Parvoviridae
Parvovirus
Pestivirus
Phlebovirus
Photobacterium
Picornaviridae
Plesiomonas
Pneumovirus
Polyomavirus
Poxviridae
Prion
Propionibacteriaceae
Propionibacterium
Propionibacterium acnes
Rabies virus

Reoviridae
Retroviridae
Rhabdoviridae
Rhinovirus
Rhodococcus
Rickettsiaceae
Rotavirus
Rubella virus
Rubivirus
Spirochaetaceae
Spumavirus
Tick-borne encephalitis virus
Togaviridae
Treponema
Trichomonacides
Ureaplasma
Uukuniemi virus
Vesicular stomatitis virus
Vibrio
Vibrio cholerae
Vibrionaceae
Yersinia
Yersinia enterocolitica
Yersinia pestis
Yersinia pseudotuberculosis
Yersinia ruckeri
(bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

IT Virus
(hepatotropic; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

IT Entamoeba
(infestation with, Dysentery, amebic; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

IT Leishmania
(leishmaniasis from; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

IT RNA viruses
(oncogenic; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

IT Virus
(oncovirus; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

IT Functional groups
(phosphonate group; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

IT Pneumonia
(pneumocytosis; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

IT Infection
(sleeping sickness; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

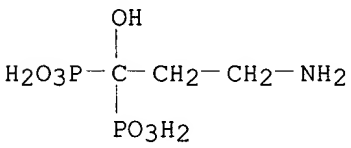
IT Toxoplasma gondii
(toxoplasmosis from; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

IT 13598-36-2D, Phosphonic acid, bisphosphonate derivs. **40391-99-9** **40391-99-9D**, derivs. **41003-10-5** **41003-10-5D**, derivs. **66376-36-1** **66376-36-1D**, derivs. **79778-41-9** **79778-41-9D**, derivs. **89130-99-4** **89130-99-4D**, derivs. **89987-06-4** **89987-06-4D**, derivs. **105462-23-5** **105462-23-5D**, derivs. **114084-78-5** **114084-78-5D**, derivs. **118072-93-8** **118072-93-8D**, derivs. **124351-85-5** **124351-85-5D** , derivs. **253265-92-8** **253265-92-8D**, derivs.
RL: AGR (Agricultural use); BAC (Biological activity or effector, except

adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

IT **40391-99-9**
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

RN 40391-99-9 HCAPLUS
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 2 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:301 HCAPLUS
DN 132:69329
TI Medicaments containing bisphosphonic acids and their derivatives for prophylaxis and treatment of **autoimmune** diseases and **allergies**
IN **Jomaa, Hassan**
PA Germany
SO Ger. Offen., 10 pp.
CODEN: GWXXBX
DT Patent
LA German
IC ICM C07F009-40
ICS C07F009-58; C07F009-6506; A61K031-66; A61K031-675; A61K045-00
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19828450	A1	19991230	DE 1998-19828450	19980626 <--
	WO 2000000182	A2	20000106	WO 1999-DE1844	19990624 <--
	WO 2000000182	A3	20000330		
	W: AL, AU, BB, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LK, LT, LV, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9955033	A1	20000117	AU 1999-55033	19990624 <--
PRAI	DE 1998-19828450	19980626 <--			
	WO 1999-DE1844	19990624			

OS MARPAT 132:69329
AB Bisphosphonic acids and their derivs. A3OP(O)(OA4)CR1(XR2)P(O)(OA1)OA2 [A1-A4 = H, (substituted) alkyl, (substituted) aryl, (substituted) aralkyl, (substituted) cycloalkyl, (substituted) heterocyclyl, metal of groups IA, IIA, or IIIA, (substituted) ammonium; X = bond, alkylene, alkenylene, hydroxyalkylene; R1, R2 = H, OH, NH2, (substituted) acyl, (substituted) alkyl, (substituted) aryl, (substituted) cycloalkyl, (substituted) aralkyl, (substituted) heterocyclyl, Cl, SR3, NR3R4; R3, R4 = H, OH, NH, (substituted) acyl, (substituted) alkyl, (substituted) aryl, (substituted) cycloalkyl, (substituted) aralkyl, (substituted) heterocyclyl], as well as their salts, esters, and prodrugs, in combination with the appropriate autoantigens or **allergens** or their fragments, derivs., or analogs thereof, are useful for reinduction of immune tolerance to autoantigens and **allergens**, and thus for prophylaxis and treatment of **autoimmune** diseases and **allergies**. The bisphosphonate and the autoantigen or **allergen** may be administered simultaneously or sequentially.

Thus, tablets for treatment of **multiple sclerosis** contained di-Na 3-amino-1-hydroxypropylidene-1,1-bisphosphonate 600, myelin basic protein 8, mannitol 400, starch 50, and Mg stearate 10 mg.

ST **autoimmune** disease treatment bisphosphonate autoantigen; **allergy** inhibitor bisphosphonate **allergen**; immune tolerance induction bisphosphonate autoantigen

IT Intestine, **disease**
(**Crohn's**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune diseases** and **allergies**)

IT **Stomach, disease**
(**atrophic gastritis, autoimmune**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)

IT DNA
Myelin basic protein
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(autoantigen; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)

IT Adrenal cortex
Heart
Hematopoietic precursor cell
Intestine
Liver
Muscle
Nervous system
Pancreatic islet of Langerhans
Skin
Stomach
(autoantigens of; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)

IT Antigens
Arrestins
Cholinergic receptors
Intrinsic factors
Thyroglobulin
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(autoantigens; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)

IT **Stomach**, disease
(**autoimmune gastritis, atrophic**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)

IT **Anemia (disease)**
(**autoimmune hemolytic anemia**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)

IT **Thyroid gland, disease**
(**autoimmune thyroiditis**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)

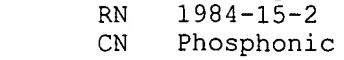
IT **Eye, disease**
(**autoimmune uveitis**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)

IT Drug delivery systems
(capsules; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)

IT Drug delivery systems
(inhalants; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT Eye
(lens, autoantigens of; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT **Addison's disease**
Allergy inhibitors
Antidiabetic agents
Antirheumatic agents
Autoimmune disease
Dermatomyositis
Lupus erythematosus
Multiple sclerosis
Myasthenia gravis
(medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune diseases** and **allergies**)
IT **Allergens**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT **Heart, disease**
(**myocarditis**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT Drug delivery systems
(ointments; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT Stomach
(parietal cell, autoantigens of; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT **Skin, disease**
(**pemphigoid**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT **Skin, disease**
(**pemphigus vulgaris**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT **Pericardium**
(**pericarditis**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT **Anemia (disease)**
(**pernicious anemia**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT **Muscle, disease**
(**polymyositis**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT **Biliary tract**
(**primary biliary cirrhosis**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT **Connective tissue**
(**scleroderma**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)

IT Drug delivery systems
(solids; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT Drug delivery systems
(solns.; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT Drug delivery systems
(sprays; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT Drug delivery systems
(tablets; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT **Immune** tolerance
(to autoantigens and **allergens**, induction of; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT Collagens, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type I, autoantigens; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT Collagens, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type II, autoantigens; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT Collagens, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type III, autoantigens; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT **Intestine, disease**
(**ulcerative colitis**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT **Hepatitis**
(**viral, chronic active**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT 11061-68-0, Human insulin
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(autoantigen; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
IT **1984-15-2D**, Methanebisphosphonic acid, derivs. **57248-88-1 121268-17-5 138926-19-9**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
RE.CNT 1
RE
(1) Anon; EP 594857 A1 HCAPLUS
IT **1984-15-2D**, Methanebisphosphonic acid, derivs.
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(medicaments contg. bisphosphonic acids and their derivs. for

prophylaxis and treatment of **autoimmune** diseases and **allergies**)
RN 1984-15-2 HCAPLUS
CN Phosphonic acid, methylenebis- (9CI) (CA INDEX NAME)



L137 ANSWER 3 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:565914 HCAPLUS
DN 131:165317
TI Use of a cardiac purinoceptor to effect cellular glucose uptake
IN Liang, Bruce T.; Birnbaum, Morris; Harden, Kendall
PA The Trustees of the University of Pennsylvania, USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-505
ICS A61K031-52; A61K031-53
CC **1-8** (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9943326	A1	19990902	WO 1999-US3881	19990223 <--
	W: AU, CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9927818	A1	19990915	AU 1999-27818	19990223 <--
PRAI	US 1998-75678		19980224 <--		
	WO 1999-US3881		19990223		

AB The invention provides a method of detg. whether a compd. is a glucose uptake modulator, including use of a cell comprising an isolated nucleic acid encoding a glucose uptake-enhancing myocardial purinoceptor. The invention also includes (1) a method of enhancing glucose uptake into a mammalian cardiac myocyte by contacting the myocyte and agonists of glucose uptake-enhancing cardiac P2Y2 and P2Y4 purinoceptors, (2) a method of increasing the activity of an intracellular enzyme selected from the group consisting of phospholipase C, protein kinase C, and phosphatidylinositol 3-kinase, and (3) pharmaceutical compns. for use in these methods. The method of enhancing glucose uptake into a cell may be used to minimize ischemic cardiac damage, such as that attributable to angina pectoris, chronic stable angina, unstable angina, post-myocardial infarction angina, myocardial infarction, cardiac arrhythmia, coronary artery disease, **diabetes mellitus**, and cardiac ischemia attributable to shock, stress, or exertion. ATP was capable of inducing more than a 3-fold enhancement of intracellular inositol phosphate prodn. in cardiac myocytes. This observation was consistent with the presence on the cells of a P2 purinergic receptor, the receptor being capable of stimulating phospholipase C (PLC) activity in cardiac myocytes. Treatment of myocytes with pertussis toxin had no effect on the ability of ATP to enhance inositol phosphate prodn., suggesting that Gq protein is involved in ATP-mediated enhancement of PLC activity. It was obsd. that ATP is capable of increasing the contractile amplitude of the cardiac myocytes. Treating cardiac myocytes with 2-methylthio-ATP, a P2 purinoceptor agonist, caused an increase in contractile amplitude similar to that caused by treating myocytes with ATP. However, 2-methylthio-ATP was not capable of enhancing intracellular PLC activity in myocyte. Furthermore, the increase in contractile amplitude of myocytes mediated by 2-methylthio-ATP was not prevented by treatment with an inhibitor of PLC. Therefore, the P2 receptor which is capable of enhancing intracellular PLC activity appears to be different from the receptor(s) which is capable of enhancing cardiac myocyte contractile amplitude.
ST cardioprotectant purinoceptor agonist insulin glucose transport

IT Transport proteins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(GLUT-1 (glucose-transporting, 1), translocation of; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)

IT Transport proteins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(GLUT-4 (glucose-transporting, 4), translocation of; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)

IT G proteins (guanine nucleotide-binding proteins)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(Gq; Gq protein in cardioprotection by agonists of purinoceptor P2Y2 and P2Y4)

IT Purinoceptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(P2U; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)

IT Purinoceptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(P2Y, P2Y4; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)

IT Swine
(Yucatan miniature, myocytes of diabetic minipig; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes)

IT Heart, disease
(angina pectoris; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)

IT Heart, disease
(arrhythmia; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)

IT Anti-ischemic agents
Diabetes mellitus
Drug delivery systems
Purinoceptor agonists
(cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)

IT Exercise
Shock (circulatory collapse)
Stress, animal
Surgery
(cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia of different origin)

IT Cytoprotective agents
(cardioprotective; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)

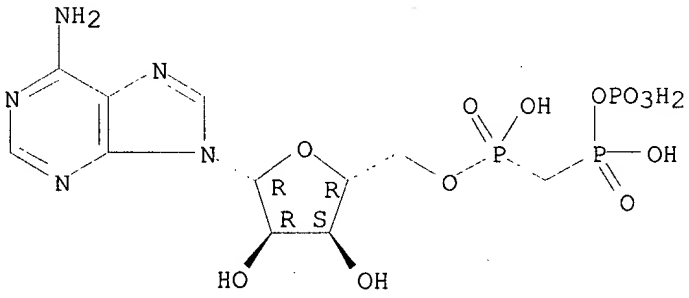
IT Artery, disease
(coronary; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)

IT Muscle
(fiber; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes)

IT Biological transport
(glucose; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
IT Heart, disease
(infarction; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
IT Heart, disease
(ischemia; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
IT Heart
(myocyte; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes)
IT Nucleic acids
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(purinoceptor-encoding; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
IT Interleukin 1 receptor antagonist
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(translocation of; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
IT Heart
(ventricle, myocyte; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes)
IT 9001-86-9, Phospholipase C 115926-52-8, Phosphatidylinositol 3-kinase 141436-78-4, Protein kinase C
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(activation of; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
IT 50-99-7, Glucose, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
IT 56-65-5, 5'-ATP, biological studies 63-39-8, 5'-UTP 63-39-8D, UTP, analogs 5542-28-9, Diadenosine tetraphosphate **7292-42-4**, .alpha.,.beta.-Methylene-adenosine 5'-triphosphate 7440-09-7, Potassium, biological studies 9004-10-8, Insulin, biological studies 35094-46-3, Adenosine 5'-(.gamma.-thio)triphosphate 43170-89-4, 2-Methylthio-adenosine 5'-triphosphate 79049-97-1, Uridine 5'-(.gamma.-thio)triphosphate
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
IT 9001-15-4, Creatine kinase
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
IT 50-99-7, D-Glucose, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(transport; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)

RE.CNT 7
RE
(1) Liang; US 5712258 A 1998 HCAPLUS
(2) Liang; US 5859019 A 1999 HCAPLUS
(3) Scamps; Circ Research 1990, V67, P1007 HCAPLUS
(4) Tang; Am J Physiol 1996, V270, PE504 HCAPLUS
(5) Tsuchida; Circ Res 1994, V75(3), P576 HCAPLUS
(6) Vergauwen; Journal of Clinical Investigation 1994, V93, P974 HCAPLUS
(7) Williams, M; Ann Rev of Pharmacology and Toxicology 1987, V27, P316
IT **7292-42-4**, .alpha.,.beta.-Methylene-adenosine 5'-triphosphate
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
RN 7292-42-4 HCAPLUS
CN Adenosine, 5'-[hydrogen [[hydroxy(phosphonooxy)phosphinyl]methyl]phosphonate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L137 ANSWER 4 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:529179 HCAPLUS
DN 131:169290
TI Treating and diagnosing macrophage-mediated diseases using Fc receptor ligands
IN Van de Winkel, Jan G. J.
PA Medarex, Inc., USA
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K016-28
ICS A61K047-48; G01N033-68
CC **15-3** (Immunochemistry)
Section cross-reference(s): 4
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9941285	A1	19990819	WO 1999-US3488	19990217 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9927721	A1	19990830	AU 1999-27721	19990217 <--
EP 1056781	A1	20001206	EP 1999-908236	19990217 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

NO 2000004098 A 20001002 NO 2000-4098 20000816 <--
PRAI US 1998-74967 19980217 <--
WO 1999-US3488 19990217

AB The invention provides methods and compns. for selectively targeting macrophages in a localized area. The compns. of the invention include an Fc receptor binding agent, e.g. anti-Fc receptor antibody conjugated to a toxin or a detectable agent. Methods for depleting or inhibiting the activity of macrophages using the compns. of the invention are disclosed. The compns. of the invention can be used therapeutically and diagnostically.

ST antibody Fc receptor toxin label macrophage

IT Ricins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A, conjugates; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Animal cell line
(ATCC CRL1117; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Immunoglobulin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgA; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Immunoglobulin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgG type I; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Immunoglobulin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgG type II; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Immunoglobulin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgG type III; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Immunoglobulin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgG; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Granulomatous disease
(Wegener's granulomatosis; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Animal tissue culture
Colorimetry
Fluorometry
Luminescence spectroscopy
Macrophage
Multiple sclerosis
Psoriasis
Rheumatoid arthritis
(anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Immunoglobulin receptors
Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

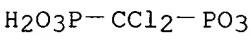
IT Dermatitis
(atopic; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Radiochemical analysis
(autoradiog., anal.; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Drug delivery systems
(carriers; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Chemistry
(chem. compds., macrophage-binding; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT Lung, disease
(chronic obstructive; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT Skin, disease
(chronic polymorphic light; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT Labels
(conjugate; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT Antibodies
Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT **Lupus erythematosus**
(cutaneous; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(exotoxin A, conjugates; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT Human immunodeficiency virus
(infection; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT Drug delivery systems
(injections, s.c.; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT Encapsulation
(liposome; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT Drug delivery systems
(liposomes; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT Growth factors, animal
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(macrophage secretion; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT Disease, animal
(macrophage-mediated; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, conjugates; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT Cell proliferation
(regulator; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(saporins, conjugates; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT **Connective tissue**
(**scleroderma**; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT Drug delivery systems
(topical; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT Drug delivery systems
(transdermal; anti-Fc receptor antibody conjugated to toxin or label

for diagnosis and treatment of macrophage-mediated diseases)
IT 9001-99-4D, Onconase, conjugates **10596-23-3D**, derivs.
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
IT 75037-46-6, Gelonin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
RE.CNT 5
RE
(1) Fanger, M; US 5635600 A 1997 HCAPLUS
(2) Kaminski, N; Journal of Immunopharmacology 1986, V8(1), P15 HCAPLUS
(3) Tempest, P; WO 9410332 A 1994 HCAPLUS
(4) Univ Pennsylvania; WO 9509002 A 1995 HCAPLUS
(5) Winkel, J; WO 9809647 A 1998 HCAPLUS
IT **10596-23-3D**, derivs.
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
RN 10596-23-3 HCAPLUS
CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 5 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:52239 HCAPLUS
DN 130:262281
TI Cyclical etidronate increases bone density in the spine and hip of postmenopausal women receiving long term corticosteroid treatment. A double blind, randomized placebo controlled study
AU Geusens, Piet; Dequeker, Jan; Vanhoof, Johan; Stalmans, Rita; Boonen, Steven; Joly, Jo; Nijs, Jos; Raus, Jef
CS L Willems-Instituut, Limburgs Universitair Centrum, Diepenbeek, B-3590, Belg.
SO Ann. Rheum. Dis. (**1998**), 57(12), 724-727
CODEN: ARDIAO; ISSN: 0003-4967
PB BMJ Publishing Group
DT Journal
LA English
CC 2-4 (Mammalian Hormones)
AB Objective: To study the effect of cyclic etidronate in secondary prevention of corticosteroid induced osteoporosis. Methods: A double blind, randomized placebo controlled study comparing cyclic etidronate and placebo during two years in 37 postmenopausal women receiving long term corticosteroid treatment, mainly for polymyalgia rheumatica (40% of the patients) and rheumatoid arthritis (30%). Bone d. was measured in the lumbar spine, femoral neck, and femoral trochanter. Results: After two years of treatment there was a significant difference between the groups in mean per cent change from baseline in bone d. in the spine in favor of etidronate ($p=0.003$). The estd. treatment difference (mean (SD)) was 9.3 (2.1)%. Etidronate increased bone d. in the spine (4.9 (2.1)%, $p<0.05$) whereas the placebo group lost bone (-2.4 (1.6)%). At the femoral neck there was an estd. difference of 5.3 (2.6)% between the groups (etidronate: 3.6 (1.4)%, $p<0.05$, placebo: -2.4 (2.1)%). The estd. difference at the trochanter was 8.2 (3.0) (etidronate: 9.0 (1.5)%, $p<0.0001$, placebo: 0.5 (2.3)%). No significant bone loss occurred in the hip in placebo treated patients. Conclusion: Cyclic etidronate is an effective treatment for postmenopausal women receiving corticosteroid treatment and is well tolerated.
ST cyclical etidronate corticosteroid induced osteoporosis postmenopause; rheumatic conditions corticosteroid induced osteoporosis postmenopause cyclical etidronate

IT Antiarthritics
Antiosteoporotic agents
Drug toxicity
Hip
Postmenopause
Rheumatoid arthritis
Spine (vertebral column)
(cyclical etidronate increases bone d. in spine and hip of postmenopausal women receiving long term corticosteroid treatment for rheumatic conditions)
IT Corticosteroids, biological studies
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclical etidronate increases bone d. in spine and hip of postmenopausal women receiving long term corticosteroid treatment for rheumatic conditions)
IT Muscle diseases
(polymyalgia rheumatica; cyclical etidronate increases bone d. in spine and hip of postmenopausal women receiving long term corticosteroid treatment for rheumatic conditions)
IT 50-24-8, Prednisolone
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclical etidronate increases bone d. in spine and hip of postmenopausal women receiving long term corticosteroid treatment for rheumatic conditions)
IT **2809-21-4**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclical etidronate increases bone d. in spine and hip of postmenopausal women receiving long term corticosteroid treatment for rheumatic conditions)
RE.CNT 27
RE
(1) Adachi, J; J Rheumatol 1994, V21, P1922 MEDLINE
(2) Adachi, J; J Rheumatol 1996, V23, P995 HCAPLUS
(3) Adachi, J; N Engl J Med 1997, V337, P382 HCAPLUS
(4) Adinoff, A; N Engl J Med 1983, V309, P265 MEDLINE
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(6) Bijlsma, J; Clin Exp Rheumatol 1988, V6, P113 MEDLINE
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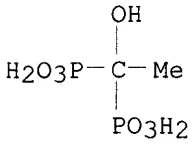
(16) Hooyman, J; Arthritis Rheum 1984, V27, P1353 MEDLINE
(17) Mulder, H; Br J Rheumatol 1994, V33, P348 MEDLINE
(18) Reid, I; Am J Clin Nutr 1986, V44, P287 MEDLINE
(19) Reid, I; Lancet 1988, Vii, P1144
(20) Saag, K; N Engl J Med 1998, V339, P292 HCAPLUS
(21) Sambrook, P; J Bone Miner Res 1990, V5, P1211 MEDLINE
(22) Sambrook, P; N Engl J Med 1993, V328, P1747 MEDLINE
(23) Sebaldt, R; Scand J Rheumatol 1996, V25(suppl 3), P91
(24) Storm, T; N Engl J Med 1990, V322, P1265 MEDLINE
(25) Struys, A; Am J Med 1994, V99, P235
(26) Verhoeven, A; J Rheumatol 1997, V24, P1495 HCAPLUS
(27) Walsch, L; BMJ 1996, V313, P344
IT **2809-21-4**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclical etidronate increases bone d. in spine and hip of postmenopausal women receiving long term corticosteroid treatment for

rheumatic conditions)
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

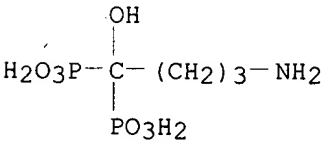


L137 ANSWER 6 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:27846 HCAPLUS
DN 130:66812
TI Tartrate salt of a substituted dipeptide as growth hormone secretagogue
IN Carpino, Philip Albert; Dasilva-Jardine, Paul Andrew; Lefker, Bruce Allen; Murry, Jerry Anthony
PA Pfizer Products Inc., USA
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K005-023
ICS A61K038-06; C07D401-06; C07D471-04; C07D471-04; C07D231-00; C07D221-00
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): **1**, 2, **63**
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9858948	A1	19981230	WO 1998-IB874	19980605 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9874455	A1	19990104	AU 1998-74455	19980605 <--
EP 989993	A1	20000405	EP 1998-921681	19980605 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9810623	A	20000725	BR 1998-10623	19980605 <--
JP 2000514840	T2	20001107	JP 1999-504027	19980605 <--
NO 9906469	A	20000223	NO 1999-6469	19991223 <--

PRAI US 1997-50723 19970625 <--
WO 1998-IB874 19980605 <--
OS MARPAT 130:66812
AB Growth hormone secretagogue 2-amino-N-{1-(2,4-difluorobenzyloxymethyl)-2-oxo-2-[3-oxo-3a-pyridin-2-ylmethyl-2-(2,2,2-trifluoroethyl)-2,3,3a,4,6,7-hexahydropyrazolo[4,3-c]pyridin-5-yl]ethyl}-2-methylpropionamide L-tartrate was prepd. The synthesis involved reactions of 4-oxopiperidine-1,3-dicarboxylic acid 1-tert-Bu, 3-Et ester, picolyl chloride hydrochloride, CF3CH2NHNH2, N-Boc-D-serine, 2,4-difluorobenzyl bromide, 2-tert-butoxycarbonylamino-2-methylpropionic acid 2,5-dioxopyrrolidin-1-yl ester, and tartaric acid.
ST dipeptide tartrate prepn growth hormone secretagogue
IT Adrenoceptor agonists
Aging (animal)
Heart failure
Hyperglycemia
Insulin dependent diabetes mellitus
Non-insulin-dependent diabetes mellitus

Obesity
Osteoporosis
Sleep disorders
(prepn. of substituted dipeptide tartrate as growth hormone secretagogue)
IT Peptides, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of substituted dipeptide tartrate as growth hormone secretagogue)
IT Conjugated estrogens
Estrogens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of substituted dipeptide tartrate as growth hormone secretagogue)
IT 5042-30-8, 2,2,2-Trifluoroethylhydrazine 6368-20-3 6959-47-3, Picolyl chloride hydrochloride 23915-07-3, 2,4-Difluorobenzyl bromide 98977-34-5 104055-39-2
RL: RCT (Reactant)
(prepn. of substituted dipeptide tartrate as growth hormone secretagogue)
IT 193272-70-7P 218163-73-6P 218163-74-7P 218163-76-9P 218163-78-1P 218163-79-2P 218163-81-6P 218163-82-7P 218163-83-8P 218163-91-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of substituted dipeptide tartrate as growth hormone secretagogue)
IT 218163-71-4P 218163-84-9P 218163-87-2P 218163-89-4P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted dipeptide tartrate as growth hormone secretagogue)
IT 57-83-0, Progesterone, biological studies 9007-12-9, Calcitonin 10540-29-1, Tamoxifen **66376-36-1**, Alendronate 82413-20-5, Droloxifene 84449-90-1, Raloxifene **114084-78-5**, Ibandronate 116057-75-1, Idoxifene 180915-78-0 180915-84-8 180915-86-0 180916-14-7 180916-15-8 180916-16-9 193274-89-4
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(prepn. of substituted dipeptide tartrate as growth hormone secretagogue)
RE.CNT 3
RE
(1) Merck & Co Inc; WO 9413696 A 1994 HCAPLUS
(2) Morriello, G; WO 9513069 A 1995 HCAPLUS
(3) Pfizer; WO 9724369 A 1997 HCAPLUS
IT **66376-36-1**, Alendronate
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(prepn. of substituted dipeptide tartrate as growth hormone secretagogue)
RN 66376-36-1 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 7 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:731646 HCAPLUS
DN 130:133755
TI Skin reactions associated with bisphosphonates: a report of 3 cases and an approach to management
AU Phillips, Elizabeth; Knowles, Sandra; Weber, Elizabeth; Shear, Neil H.
CS Departments of Medicine (Clinical Pharmacology, Sunnybrook Health Science

Centre, Toronto, ON, Can.
SO J. Allergy Clin. Immunol. (**1998**), 102(4, Pt. 1), 697-698
CODEN: JACIBY; ISSN: 0091-6749
PB Mosby, Inc.
DT Journal
LA English
CC **1-6** (Pharmacology)
AB The cutaneous reactions assocd. with bisphosphonate therapy in patients with breast cancer and the management of these reactions were reported in 3 cases. The cutaneous reactions to clodronate and pamidronate appear to be IgE-mediated and include urticaria, angioedema, hypotension, and (or) tachycardia occurring within 48 h after initiation of treatment. Oral challenge and desensitization with alendronate, a bisphosphonate structurally similar to pamidronate, allowed 2 of the patients to continue using this class of medication. The usefulness of skin testing for bisphosphonate reactions need to be validated, since the haptens that may be involved in IgE-mediated reactions to these drugs are unknown, as is the predictive value of the parent compds. as skin-testing material.
ST clodronate pamidronate alendronate etidronate bisphosphonate anticancer
IT **Allergies**
Breast tumor inhibitors
(skin reactions assocd. with bisphosphonate treatment in breast cancer patients)
IT IgE
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(skin reactions assocd. with bisphosphonate treatment in breast cancer patients)
IT **10596-23-3 40391-99-9 66376-36-1**, Alendronate
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(skin reactions assocd. with biphosphonate treatment in breast cancer patients)
IT **2809-21-4** 13598-36-2D, Phosphonic acid, alkylidenebis- derivs.
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(skin reactions assocd. with bisphosphonate treatment in breast cancer patients)
RE.CNT 6
RE
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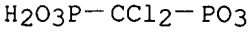
(3) Mautalen, C; Br Med J 1984, V288, P828 MEDLINE
(4) Nakamura, M; Br J Pharmacol 1996, V119, P205 HCAPLUS
(5) Pajus, I; Br Med J 1993, V307, P484 MEDLINE
(6) Roux, C; Calcif Tissue Int 1992, V50, P78
IT **10596-23-3**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(skin reactions assocd. with biphosphonate treatment in breast cancer patients)
RN 10596-23-3 HCAPLUS
CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 8 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:706502 HCAPLUS
DN 130:90420
TI Liposome-encapsulated Clodronate retards the development of experimental

autoimmune uveitis

AU Niesman, Michael R.; Ni, Ming; Bloom, Jeffrey N.
CS Agouron Pharmaceuticals, San Diego, CA, 92121, USA

SO J. Liposome Res. (**1998**), 8(3), 367-379
CODEN: JLREE7; ISSN: 0898-2104
PB Marcel Dekker, Inc.
DT Journal
LA English
CC **1-11** (Pharmacology)
Section cross-reference(s): 14, **15**, **63**

AB A study was undertaken to det. if the i.v. injection of liposome-encapsulated dichloromethylene diphosphonate (Cl2MDP; Clodronate), a treatment known to deplete monocytes, as well as liver and spleen macrophages, would reduce the no. of macrophages in the retina of animals with exptl. **autoimmune uveitis** (EAU) and decrease the severity of the disease. EAU was induced in Lewis rats by immunization with S-antigen (S-Ag). Monocytes and macrophages were depleted via an i.v. injection of Cl2MDP encapsulated in liposomes. Control groups included rats that received no S-Ag (n=18), S-Ag and no treatment (n=23), S-Ag and free drug (n=20), or empty liposomes (n=14). Treated animals received injections of the Cl2MDP-liposomes, free drug, or empty liposomes. Animals were sacrificed at 14, 21 and 28 days post-S-Ag administration. I.v., Cl2MDP-liposomes produced a statistically significant redn. in the severity of the EAU when compared to controls at both days 14 and 21 following S-Ag injection. Immunohistochem. staining with the monoclonal antibody ED1 demonstrated that the severity of the ocular inflammatory response correlated with the no. of ED1-pos. cells in the retina. Following the cessation of treatment, treated animals developed disease that was as severe at day 28 as that of untreated animals at day 21. These results confirm the importance of monocytes and macrophages in EAU by demonstrating the correlation between the presence of ED1-pos. cells in the retina and the resultant damage to the retina. Although the dosing regimen employed here did not provide a cure, strategies designed to prevent the local recruitment and/or activation of mononuclear phagocytes may prove to be useful in the treatment of EAU.

ST Clodronate liposome **autoimmune uveitis** treatment
IT **Uveitis**
(**autoimmune**; liposome-encapsulated Clodronate retards the development of exptl. **autoimmune uveitis** by depletion of monocytes and macrophages)
IT Liposomes (drug delivery systems)
Macrophage
Monocyte
(liposome-encapsulated Clodronate retards the development of exptl. **autoimmune uveitis** by depletion of monocytes and macrophages)
IT **Autoimmune diseases**
(**uveitis**; liposome-encapsulated Clodronate retards the development of exptl. **autoimmune uveitis** by depletion of monocytes and macrophages)
IT **10596-23-3**
RL: BAC (Biological activity or effector, except adverse); **THU** (**Therapeutic use**); BIOL (Biological study); USES (Uses)
(liposome-encapsulated Clodronate retards the development of exptl. **autoimmune uveitis** by depletion of monocytes and macrophages)

RE.CNT 30
RE
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(4) Claassen, E; J Microencaps 1986, V3, P109 HCAPLUS
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(15) Huitinga, I; Clin Exp Immunol 1995, V100, P344 MEDLINE
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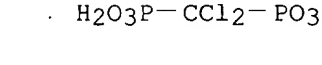
(28) van Lent, P; Res Immunol 1992, V143, P229 HCAPLUS
(29) van Rooijen, N; J Immuno Meth 1989, V124, P1 HCAPLUS
(30) Vidal, M; Embo J 1985, V4, P2461 HCAPLUS

IT **10596-23-3**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(liposome-encapsulated Clodronate retards the development of exptl. **autoimmune uveitis** by depletion of monocytes and macrophages)

RN 10596-23-3 HCAPLUS

CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)



$H_2O_3P-CCl_2-PO_3H_2$

L137 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:574148 HCAPLUS

DN 129:339833

TI Effects of alendronate sodium on severe osteodystrophy in postmenopausal patients with **primary biliary cirrhosis**: a pilot study

AU Floreani, Annarosa; Tizian, Luisa; Luisetto, Giovanni; Buda, Andrea; Mega, Andrea; Naccarato, Remo

CS Department of Gastroenterology, University of Padova, Padua, 35100, Italy

SO Curr. Ther. Res. (**1998**), 59(8), 589-593
CODEN: CTCEA9; ISSN: 0011-393X

PB Excerpta Medica

DT Journal

LA English

CC **1-12** (Pharmacology)

AB Osteodystrophy is a major complication in **primary biliary cirrhosis** (PBC) and a significant problem for patients who require a liver transplant. Treatment for osteodystrophy has yet to be standardized. The goal of this pilot study was to assess the efficacy and tolerability of alendronate sodium, a potent specific inhibitor of osteoclast-mediated bone resorption. The study comprised 15 postmenopausal PBC patients (mean age, 64.25 .+-. 8.77 yr) with severe osteodystrophy. Four patients had histol. stage II disease, 8 stage III, and 3 stage IV. All patients had a T score below 2, indicating a fracture risk of 60%. All patients received two courses of alendronate sodium (10 mg/d for 3 mo, sepd. by a 2-mo interval). The following variables were assessed at baseline and after 10 mo: bone mineral d. (BMD) (by dual-energy x-ray absorptiometry in the lumbar spine), calcium, sodium, potassium, creatinine, 25-hydroxyvitamin D, parathyroid hormone, and osteocalcin. No patients dropped out of the study, and therapy was well

tolerated by all patients. At the end of treatment, BMD increased significantly compared with baseline (0.714 .+-. 0.115 g/cm2 vs 0.740 .+-. 0.108 g/cm2). Although not statistically significant, a trend toward an increase in serum osteocalcin levels (1.4 .+-. 1.5 ng/mL vs 2.6 .+-. 1.4 ng/mL) was evident. These preliminary findings suggest that alendronate sodium may be helpful in treating severe osteodystrophy in postmenopausal patients with PBC. Larger, controlled trials using long-term treatment with alendronate sodium are needed to establish the efficacy and safety of this drug.

ST alendronate sodium osteodystrophy postmenopause

IT Postmenopause
(effects of alendronate sodium on severe osteodystrophy in postmenopausal humans with **primary biliary cirrhosis**)

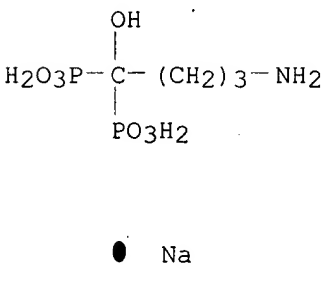
IT Bone diseases
(osteodystrophy, inhibitors; effects of alendronate sodium on severe osteodystrophy in postmenopausal humans with **primary biliary cirrhosis**)

IT **129318-43-0**, Alendronate sodium
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(effects of alendronate sodium on severe osteodystrophy in postmenopausal humans with **primary biliary cirrhosis**)

IT **129318-43-0**, Alendronate sodium
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(effects of alendronate sodium on severe osteodystrophy in postmenopausal humans with **primary biliary cirrhosis**)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI) (CA INDEX NAME)



L137 ANSWER 10 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:542529 HCAPLUS

DN 129:254608

TI Effect of combined cyclosporine A and liposome encapsulated dichloromethylene diphosphonate on the organization of the rat thymus: evidence for a role of macrophages in guiding the post cyclosporine A thymic reorganization

AU Rezzani, R.; Rodella, L.; Bianchi, R.

CS Department of Biomedical Sciences and Biotechnology, Division of Human Anatomy, University of Brescia, Brescia, 19-25123, Italy

SO Int. J. Immunopharmacol. (**1998**), 20(4/5), 183-192
CODEN: IJIMDS; ISSN: 0192-0561

PB Elsevier Science Ltd.

DT Journal

LA English

CC **1-7** (Pharmacology)
Section cross-reference(s): **15**

AB Cyclosporine A (CsA) is a powerful immunosuppressant inducing marked involution of the thymic medulla, and disappearance of interdigitating cells (IDCs) and reducing the no. of macrophages (M.phi.). Usually, while the thymus of rats receiving a short course of CsA promptly recovers after stopping CsA treatment, long term CsA treatment, like mediastinal irradn., impairs the normal thymic recovery and is thought to be responsible for the development of **autoimmune** diseases. In the present study we evaluated the role played by the IDCs and M.phi. in the normal recovery of the thymic histol. at light and ultrastructural level. Besides CsA administration, we also used liposome-encapsulated dichloromethylenediphosphonate (lip-CL2MDP), that induces a total depletion of the M.phi. resistant to CsA. After a short (21 days) course of CsA and lip-CL2MDP administration, we did not observe the normal recovery of the thymic parenchyma but only cortical zones consisting of lymphoblasts, epithelial cells and M.phi.. The CsA/lip-CL2MDP treatment detg. the loss of IDCs and M.phi. and consequently the loss of the normal thymic histol. seems to simulate in the rats, the long term CsA treatment or the mediastinal irradn. The results obtained suggest that the loss of IDCs and the depletion of M.phi. interfere with the normal thymic recovery. The delay in the recovery of IDCs could be a consequence of the absence of macrophages. These findings would indicate that the IDCs, detg. the neg. selection of T-lymphocytes, are the main cells responsible for the thymic microenvironment.

ST cyclosporine thymus reorganization macrophage

IT **Autoimmune diseases**
Langerhans' cell
Liposomes (drug delivery systems)
Macrophage
Thymus gland
(role of macrophages in guiding post cyclosporine A thymic reorganization)

IT 59865-13-3, Cyclosporine A
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of macrophages in guiding post cyclosporine A thymic reorganization)

IT **10596-23-3**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(role of macrophages in guiding post cyclosporine A thymic reorganization)

IT **10596-23-3**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(role of macrophages in guiding post cyclosporine A thymic reorganization)

RN 10596-23-3 HCAPLUS

CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)

$H_2O_3P-CCl_2-PO_3H_2$

L137 ANSWER 11 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:62552 HCAPLUS

DN 128:119687

TI Topical compositions containing chelators for **allergic** dermatitis

IN Ito, Masatoshi; Fujii, Masashi

PA Fujii, Masashi, Japan

SO Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF

DT Patent

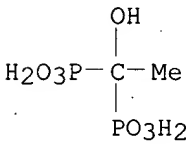
LA Japanese

IC ICM A61K045-00

ICS A61K031-195; A61K031-66; A61K033-42; C09K003-00
CC **63-6** (Pharmaceuticals)
Section cross-reference(s): **1**
FAN.CNT 1

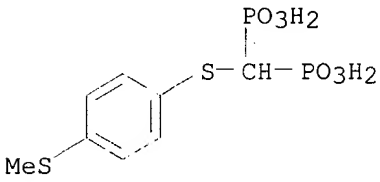
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10017493	A2	19980120	JP 1996-207532	19960702 <--

AB Topical compns. for treatment of **allergic** dermatitis contain ion chelators for calcium are claimed. An ointment contained menthol 0.1, EDTA 0.1 and white petrolatum to 100 wt.%.
ST topical pharmaceutical chelator **allergic** dermatitis
IT **Allergic** dermatitis
Chelating agents
Ointments (drug delivery systems)
Topical drug delivery systems
(topical compns. contg. chelators for treatment of **allergic** dermatitis)
IT 60-00-4, EDTA, biological studies 83-86-3, Phytic acid **2809-21-4**, Hydroxyethanediphosphonic acid
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(topical compns. contg. chelators for treatment of **allergic** dermatitis)
IT **2809-21-4**, Hydroxyethanediphosphonic acid
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(topical compns. contg. chelators for treatment of **allergic** dermatitis)
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 12 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:772117 HCAPLUS
DN 128:97459
TI The effect of TRK-530 on experimental arthritis in mice
AU Takaoka, Yuko; Nagai, Hiroichi; Mori, Hiroshi; Tanahashi, Masahiko
CS Department of Pharmacology, Gifu Pharmaceutical University, Gifu, 502, Japan
SO Biol. Pharm. Bull. (**1997**), 20(11), 1147-1150
CODEN: BPBLEO; ISSN: 0918-6158
PB Pharmaceutical Society of Japan
DT Journal
LA English
CC **1-7** (Pharmacology)
AB TRK-530 is a newly synthesized diphosphonate deriv. We investigated the effect of TRK-530 on type II collagen-induced arthritis (CIA) in mice in comparison to that of prednisolone and indomethacin. TRK-530 at a dose of 25 mg/kg showed a tendency to inhibit CIA. TRK-530 at a dose of 50 mg/kg inhibited the development of the CIA in terms of the progression of footpad swelling, bone damage and histopathol. changes. TRK-530 at a dose of 50 mg/kg also significantly inhibited the delayed type hypersensitivity (DTH) response to type II collagen, but not the prodn. of anti-type II collagen IgG antibody in arthritic mice. To investigate the inhibitory mechanism of TRK-530, the type of effect of TRK-530 on the prodn. of IL-1.beta. in vitro was studied. TRK-530 at a concn. of 10-4 M inhibited LPS-induced IL-1.beta. prodn. from J774.1 cells. In conclusion, TRK-530 inhibited CIA in mice. The inhibition of the DTH reaction to type II collagen and the inhibition of IL-1.beta. prodn. may partly participate the anti-rheumatoid action of TRK-530.

ST diphosphonate TRK530 antiarthritic antirheumatic interleukin
IT Antiarthritics
Antirheumatic drugs
(effect of diphosphonate deriv. TRK-530 on exptl. arthritis in mice)
IT **Delayed hypersensitivity**
(inhibition of; effect of diphosphonate deriv. TRK-530 on exptl. arthritis in mice)
IT Interleukin 1.beta.
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(inhibition of; effect of diphosphonate deriv. TRK-530 on exptl. arthritis in mice)
IT **151425-92-2**, TRK 530
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(effect of diphosphonate deriv. TRK-530 on exptl. arthritis in mice)
IT **151425-92-2**, TRK 530
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(effect of diphosphonate deriv. TRK-530 on exptl. arthritis in mice)
RN 151425-92-2 HCAPLUS
CN Phosphonic acid, [[[4-(methylthio)phenyl]thio]methylene]bis-, disodium salt (9CI) (CA INDEX NAME)



● 2 Na

L137 ANSWER 13 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:757141 HCAPLUS
DN 128:30414
TI Isopentenyl pyrophosphate isomerase and/or prenyl transferase inhibitors for therapeutic use
IN Brown, Richard John; Watts, Donald Jeremy; Russel, Robert Graham Goodwin; Rogers, Michael John
PA University of Sheffield, UK; Brown, Richard John; Watts, Donald Jeremy; Russel, Robert Graham Goodwin; Rogers, Michael John
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12Q
CC **1-12** (Pharmacology)
Section cross-reference(s): 5
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9743437	A2	19971120	WO 1997-GB1302	19970512	<--
	WO 9743437	A3	19980226			

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,

ML, MR, NE, SN, TD, TG
AU 9727833 A1 19971205 AU 1997-27833 19970512 <--
EP 952834 A2 19991103 EP 1997-921954 19970512 <--
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE, IE
PRAI GB 1996-10174 19960515 <--
GB 1997-8329 19970425 <--
WO 1997-GB1302 19970512 <--

AB Prenyl transferase (farnesyl pyrophosphate synthase) and/or isopentenyl pyrophosphate isomerase inhibitors find application in various forms of therapy and prophylaxis. The use of such inhibitors in the treatment of various diseases and disorders of bone metab.; in the screening, isolation, synthesis and the evaluation of osteoactive drugs; and as hypolipidemic and anti-cancer agents is also described. Herbicides and fungicides comprising prenyl transferase and/or isopentenyl pyrophosphate isomerase inhibitors are also disclosed.

ST isopentenyl pyrophosphate isomerase inhibitor therapeutic; prenyl transferase inhibitor therapeutic; bone metab disorder hypolipidemic anticancer therapeutic; herbicide fungicide prenyl transferase inhibitor; fungicide herbicide isopentenyl pyrophosphate isomerase inhibitor

IT Proteins (specific proteins and subclasses)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CaaX box-contg., prenylation; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Proteins (specific proteins and subclasses)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(Rab6; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Arterial restenosis
(after coronary angioplasty; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Familial hypercholesterolemia
(and homozygous familial hypercholesterolemia; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Coronary artery
(angioplasty, restenosis after; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Isoprenoids
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(apoptosis related to; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Bone tumors
Metastasis inhibitors
(bone metastasis inhibitors; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Antitumor agents
Metabolism
(bone; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Carboxylic acids, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carboxylates and phosphonocarboxylates; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT High-density lipoproteins
Low-density lipoproteins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(cholesterol; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Angioplasty
(coronary, restenosis after; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Liver
(dysfunction, lipid metab. modulation in; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for

therapeutic use)
IT Drug screening
(for osteoactive drugs; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
IT Proteins (general), biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(hyperproteinemia; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
IT Dipeptides
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor conjugates; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
IT Bone tumors
(inhibitors; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
IT Dictyostelium
Dictyostelium discoideum
(isopentenyl pyrophosphate isomerase and prenyl transferase; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
IT Allograft
Anti-inflammatory drugs
Antiarthritics
Antiatherosclerotics
Anticholesteremic agents
Antiosteoporotic agents
Antiproliferative agents
Antitumor agents
Apoptosis
Autoimmune diseases
Bladder carcinoma inhibitors
Bone resorption inhibitors
Brain tumor inhibitors
Cardiovascular agents
Cell proliferation
Colon tumor inhibitors
Diagnostic agents
Drug design
Farnesylation
Fungicides
Herbicides
Hypercalcemia
Hyperlipoproteinemia
Hypolipemic agents
Imaging agents
Lipid metabolic diseases
Lung tumor inhibitors
Molecular modeling
Paget's disease of bone
Prenylation
Signal transduction (biological)
Test kits
Transplant rejection
(isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
IT Diphosphates
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
IT Glycerides, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
IT LDL receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Arterial diseases
(lesion; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Macrophage
(mevastatin effect on macrophage apoptosis)

IT Hyperlipidemia
(nephrotic; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Bone
(osteoactive bisphosphonates; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Drugs
(osteoactive; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Proteins (general), biological studies
Ras proteins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prenylation; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Sulfonic acids, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfonates; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Alkenylation
(tetramethylhexadecatetraenylation; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Antibodies
Monoclonal antibodies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to isopentenyl pyrophosphate isomerase or prenyl transferase; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT 9032-79-5, Prenyl transferase 9033-27-6, Isopentenyl pyrophosphate isomerase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT **10596-23-3** 13598-36-2D, Phosphonic acid, bisphosphonates **40391-99-9 40391-99-9D**, analogs and derivs. **66376-36-1**, Alendronate **66376-36-1D**, Alendronate, analogs and derivs. **105462-24-6 114084-78-5**, Ibandronate **114084-78-5D**, Ibandronate, analogs and derivs. **138330-18-4**, YM175 199668-51-4D, analogs
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT 57-88-5, Cholesterol, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT 674-26-0, Mevalonic acid lactone 6699-20-3, Geranylgeranyl pyrophosphate 13058-04-3, Farnesyl pyrophosphate 73573-88-3, Mevastatin
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(mevastatin effect on macrophage apoptosis)

IT **10596-23-3**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

RN 10596-23-3 HCAPLUS
CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)

L137 ANSWER 14 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:735846 HCAPLUS
DN 127:341814
TI Uses of inorganic pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity
IN Welsh, Michael J.
PA University of Iowa Research Foundation, USA
SO U.S., 15 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K033-42
NCL 424601000
CC **1-12** (Pharmacology)
Section cross-reference(s): **63**
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5686114	A	19971111	US 1995-484847	19950602 <--
US 5958907	A	19990928	US 1997-920999	19970829 <--
PRAI US 1995-484847		19950602 <--		

AB Pharmaceutical compns. are disclosed which comprise an inorg. pyrophosphate (PPi) in a form that renders the PPi accessible to ABC proteins when administered to a subject in vivo; also disclosed are use of the compns. for treating subjects having a disease or disorder assocd. with inappropriate or inadequate ABC protein activity (e.g., cystic fibrosis, multidrug resistance, Zellweger's Syndrome).
ST inorg pyrophosphate pharmaceutical ABC protein disease
IT CFTR (cystic fibrosis transmembrane conductance regulator)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(508-dephenylalanine-; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)
IT Proteins (specific proteins and subclasses)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(ABC (ATP-binding cassette-contg.); inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)
IT Diseases (animal)
(ABC protein-related; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)
IT Mutation
(CFTR; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)
IT Proteins (specific proteins and subclasses)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(PMP70; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)
IT Lipidosis
Nervous system diseases
(Refsum disease, infantile; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)
IT Proteins (specific proteins and subclasses)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(TAP (transporter in antigen processing); inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)
IT MHC antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(TAP-mediated antigen presentation linked to; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT Antigen presentation
(TAP-mediated; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT Epithelium
(apical membrane; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT Drug resistance
(chemotherapeutic; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT Apical membrane
(epithelial; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT **Autoimmune diseases**
Constipation
Cystic fibrosis
Drug delivery systems
Laxatives
Transplant rejection
Zellweger syndrome
(inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT CFTR (cystic fibrosis transmembrane conductance regulator)
P-glycoproteins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT Biological simulation
(kinetic; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT Brain diseases
(neonatal adrenoleukodystrophy; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT Chemotherapy
(resistance; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT 535-75-1, Pipecolic acid
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(hyperpipecolic acidemia; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT 142008-29-5, CAMP-dependent protein kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT **1984-15-2**, Methylenediphosphonic acid **7414-83-7**, Etidronate disodium 7722-88-5 14000-31-8, Diphosphate 112319-85-4, Imidodiphosphate
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

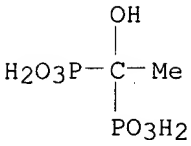
IT 56-65-5, Adenosine triphosphate, biological studies 16887-00-6, Chloride, biological studies 53696-59-6, 8-Azidoadenosine triphosphate
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT **1984-15-2**, Methylenediphosphonic acid
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

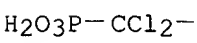
RN 1984-15-2 HCAPLUS
CN Phosphonic acid, methylenebis- (9CI) (CA INDEX NAME)

$H_2O_3P-CH_2-PO_3H_2$

L137 ANSWER 15 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:467046 HCAPLUS
DN 127:130960
TI Etidronate versus fluoride for treatment of osteopenia in **primary biliary cirrhosis**: preliminary results after 2 years
AU Guanabens, Nuria; Pares, Albert; Monegal, Ana; Peris, Pilar; Pons, Francesca; Alvarez, Luisa; De Osaba, M. Jesus Martinez; Roca, Merce; Torra, Merce; Rodes, Joan
CS Metabolic Bone Diseases Unit, Hospital Clinic i Provincial, University of Barcelona, Barcelona, Spain
SO Gastroenterology (**1997**), 113(1), 219-224
CODEN: GASTAB; ISSN: 0016-5085
PB Saunders
DT Journal
LA English
CC **1-12** (Pharmacology)
AB Because osteopenia increases morbidity of **primary biliary cirrhosis** (PBC), the effects of cyclical etidronate vs. sodium fluoride on bone mass were compared in patients with PBC. Thirty-two women with PBC were randomly assigned to receive etidronate (400 mg/day during 14 days every 3 mo) or fluoride (50 mg/day, enteric-coated tablets). Bone mineral d. of the lumbar spine and proximal femur were measured initially and every 6 mo. Bone fractures were also evaluated. Sixteen patients were allocated into each group, which were comparable with respect to the severity of PBC and osteopenia. Thirteen patients with etidronate and 10 patients with fluoride completed 2 yr in the study. In the etidronate group, bone mineral d. increased in the lumbar spine ($P = 0.02$) and did not change in the proximal femur. In the fluoride group, lumbar bone mineral d. did not change but femoral bone mass decreased, particularly in the Ward's triangle. Two patients in the fluoride and none in the etidronate group developed new vertebral fractures, and the no. of new nonvertebral fractures was similar in both groups. Neither treatment impaired liver function or cholestasis. Cyclical etidronate is more effective and better tolerated than sodium fluoride in preventing bone loss in PBC.
ST etidronate fluoride osteopenia bone loss cirrhosis
IT **Cirrhosis (liver)**
(**biliary**; etidronate vs. fluoride for treatment of osteopenia in **primary biliary cirrhosis**)
IT Osteopenia
(etidronate vs. fluoride for treatment of osteopenia in **primary biliary cirrhosis**)
IT **2809-21-4** 16984-48-8, Fluoride, biological studies
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(etidronate vs. fluoride for treatment of osteopenia in **primary biliary cirrhosis**)
IT **2809-21-4**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(etidronate vs. fluoride for treatment of osteopenia in **primary biliary cirrhosis**)
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 16 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:287320 HCAPLUS
DN 126:347199
TI Apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes. Reply to comments
AU Schmidt-Weber, C. B.; Rittig, M.; Hauser, I.; Nurnberg, E.; Emmrich, F.; Palombo-Kinne, E.; Kinne, R. W.
CS Dep. of Pathology, Immunology Research Division, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA
SO J. Leukocyte Biol. (**1997**), 61(5), 644-645
CODEN: JLBIE7; ISSN: 0741-5400
PB Federation of American Societies for Experimental Biology
DT Journal
LA English
CC **63-5** (Pharmaceuticals)
Section cross-reference(s): **1**, **15**
AB While the treatment of anatomically confined pathologies such as cancer heavily relies on liposome formulations that evade the mononuclear phagocyte system and thereby increase the availability of drug-laden liposomes to these masses, treatment of systemic inflammatory diseases may instead benefit from the use of liposomes that remain "visible" to the MPS and, in particular, to centrally located macrophage subpopulations with immunoregulatory potential.
ST clodronate liposome monocyte apoptosis **autoimmunity** polemic
IT Antiarthritics
Arthritis
Autoimmune diseases
Liposomes (drug delivery systems)
Macrophage
Monocyte
(apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes)
IT **10596-23-3**, Clodronic acid
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes)
IT **10596-23-3**, Clodronic acid
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes)
RN 10596-23-3 HCAPLUS
CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 17 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:180436 HCAPLUS
DN 126:220689
TI Cyclical etidronate in the prevention of bone loss in corticosteroid-

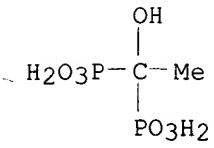
treated **primary biliary cirrhosis**: a prospective, controlled pilot study

AU Wolfhagen, Frank H. J.; Van Buuren, Henk R.; Den Ouden, Janny W.; Hop, Wim C. J.; Van Leeuwen, Johannes P. T. M.; Schalm, Solko W.; Pols, Huib A. P.
CS Department of Internal Medicine II (section Hepatology), University Hospital Rotterdam, Rotterdam, Neth.

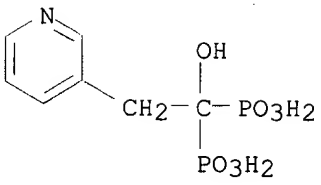
SO J. Hepatol. (**1997**), 26(2), 325-330
CODEN: JOHEEC; ISSN: 0168-8278
PB Munksgaard
DT Journal
LA English
CC **1-12** (Pharmacology)
Section cross-reference(s): 2

AB Recently, promising disease modifying effects of low dose corticosteroid treatment in **primary biliary cirrhosis** have been reported. However, steroid-induced bone loss constitutes a potential draw-back of this treatment option. To assess whether etidronate can reduce bone loss during corticosteroid treatment. Twelve **primary biliary cirrhosis** patients (all Child-Pugh Class A), treated with prednisone in the context of a 1-yr placebo-controlled pilot study with prednisone (maintenance dose 10 mg daily), and azathioprine (50 mg daily), were randomized to receive either cyclical etidronate (400 mg daily, during 2 wk) alternated with calcium 500 mg daily during 11 wk or calcium alone. All patients had been receiving ursodeoxycholic acid during at least 1 yr and this treatment was continued. Bone mass was measured in the lumbar spine and the femoral neck by dual energy X-ray absorptiometry before and after 3 and 12 mo of treatment. Markers of bone formation (serum osteocalcin, procollagen-I-propeptide) and bone resorption (urinary deoxypyridinoline and calcium) were also monitored. The mean lumbar bone mineral d. did not significantly change in the patients taking etidronate+calcium, in contrast to patients treated with calcium alone (+0.4 vs. -3.0%; p=0.01). Changes in femoral bone mineral d. and markers of bone turnover did not significantly differ between both groups. No adverse effects of etidronate were noted. Cyclical etidronate appears to prevent bone loss assocd. with prednisone treatment in patients with **primary biliary cirrhosis**. These preliminary results encourage the further evaluation of long term prednisone treatment and concurrent bisphosphonate therapy in **primary biliary cirrhosis**.

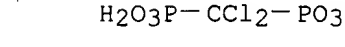
ST bone loss corticosteroid biliary cirrhosis etidronate
IT Bone demineralization
Primary biliary cirrhosis
(cyclical etidronate in prevention of bone loss in corticosteroid-treated **primary biliary cirrhosis**)
IT Corticosteroids, biological studies
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclical etidronate in prevention of bone loss in corticosteroid-treated **primary biliary cirrhosis**)
IT 53-03-2, Prednisone
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclical etidronate in prevention of bone loss in corticosteroid-treated **primary biliary cirrhosis**)
IT 128-13-2, Ursodeoxycholic acid 446-86-6, Azathioprine **2809-21-4** 7440-70-2, Calcium, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclical etidronate in prevention of bone loss in corticosteroid-treated **primary biliary cirrhosis**)
IT **2809-21-4**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclical etidronate in prevention of bone loss in corticosteroid-treated **primary biliary cirrhosis**)
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



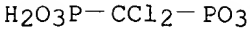
L137 ANSWER 18 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:82270 HCAPLUS
DN 126:181022
TI A double-blind placebo-controlled study to determine the effects of risedronate on bone loss in glucocorticoid-treated rheumatoid arthritis
AU Eastell, R.; Devogelaer, J. P.; Peel, N. F. A.; Gill, C.; Bax, D. E.; Nagant de Deuxchaisnes, C.; Russell, R. G. G.
CS Dep. Human Metabolism Clin. Biochem., Univ. Sheffield, Sheffield, S5 7AU, UK
SO Int. Congr. Ser. (**1996**), 1118(Osteoporosis 1996), 391-393
CODEN: EXMDA4; ISSN: 0531-5131
PB Elsevier
DT Journal
LA English
CC **1-7** (Pharmacology)
Section cross-reference(s): 2
AB Glucocorticoid therapy and rheumatoid arthritis are two independent risk factors for osteoporosis resulting together in a 6-fold increase in the risk of vertebral fractures. We performed a double-blinded, placebo-controlled trial of risedronate in 120 postmenopausal women with rheumatoid arthritis on glucocorticoids. Risedronate was given either continuously (2.5 mg/day) or cyclically (15 mg/day for 2 out of 12 wk). At 2 yr there was marked bone loss from the proximal femur in placebo-treated patients. This as well as the bone loss from the spine appeared to be prevented by risedronate treatment.
ST rheumatoid arthritis glucocorticoid bone loss risedronate; osteoporosis rheumatoid arthritis glucocorticoid therapy
IT Antirheumatic drugs
Osteoporosis
Postmenopause
Rheumatoid arthritis
(a double-blind placebo-controlled study to det. the effects of risedronate on bone loss in glucocorticoid-treated rheumatoid arthritis)
IT Glucocorticoids
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(a double-blind placebo-controlled study to det. the effects of risedronate on bone loss in glucocorticoid-treated rheumatoid arthritis)
IT **105462-24-6**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(a double-blind placebo-controlled study to det. the effects of risedronate on bone loss in glucocorticoid-treated rheumatoid arthritis)
IT **105462-24-6**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(a double-blind placebo-controlled study to det. the effects of risedronate on bone loss in glucocorticoid-treated rheumatoid arthritis)
RN 105462-24-6 HCAPLUS
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



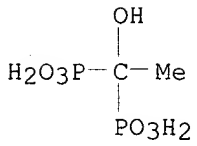
L137 ANSWER 19 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:686835 HCAPLUS
DN 126:102239
TI Malignant hematological diseases
AU Eto, Sumiya
CS Univ. Occup. Environ. Health, Kitakyushu, 807, Japan
SO Bone (Osaka) (**1996**), 10(2), 143-149
CODEN: BONEFN; ISSN: 0914-7047
PB Medikaru Rebyusha
DT Journal; General Review
LA Japanese
CC 14-0 (Mammalian Pathological Biochemistry)
Section cross-reference(s): **1**, 3, **15**
AB A review, with 33 refs., on the osteolytic lesions, hypercalcemia and bone-resorbing cytokines in multiple myeloma, adult T-cell leukemia, malignant lymphoma and **pernicious anemia**, and effects of biphosphonates.
ST review hematol disease cytokine therapy
IT Adult T-cell leukemia
Hypercalcemia
Lymphoma
Multiple myeloma
(malignant hematol. diseases and therapies in human)
IT Interleukin 1
Interleukin 6
Tumor necrosis factor .alpha.
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(malignant hematol. diseases and therapies in human)
IT **Anemia (disease)**
(**pernicious anemia**; malignant hematol. diseases and therapies in human)
IT 7440-70-2, Calcium, biological studies
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)
(malignant hematol. diseases and therapies in human)
IT 103370-86-1, Humoral hypercalcemic factor
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(malignant hematol. diseases and therapies in human)
IT **10596-23-3 40391-99-9**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(malignant hematol. diseases and therapies in human)
IT **10596-23-3**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(malignant hematol. diseases and therapies in human)
RN 10596-23-3 HCAPLUS
CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 20 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:542252 HCAPLUS
DN 125:230474
TI Apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes
AU Schmidt-Weber, Carsten; Rittig, Michael; Buchner, Eberhard; Hauser, Ingeborg; Schmidt, Irina; Palombo-Kinne, Ernesta; Emmrich, Frank; Kinne, Raimund W.
CS Immunol. Unit, Dep. Medicine III, Univ. Erlangen-Nuremberg, Leipzig, Germany
SO J. Leukocyte Biol. (**1996**), 60(2), 230-244
CODEN: JLBIE7; ISSN: 0741-5400
DT Journal
LA English
CC **63-5** (Pharmaceuticals)
Section cross-reference(s): **1, 15**
AB The present study was performed to elucidate whether sterically stabilized liposomes laden with clodronate, which lead to depletion of macrophages (M.PHI.s) and amelioration of exptl. **autoimmune** arthritis in vivo, selectively affect cells of the m.PHI. lineage in vitro. The rates of incorporation of drug-free, fluorescent liposomes and the rates of cell death following exposure to clodronate-liposomes were assessed in human peripheral blood monocytes, as well as in polymorphonuclear leukocytes (PMNs), T cells, endothelial cells, and fibroblasts, both at rest and following activation. Gel electrophoresis of nuclear exts. and ultrastructural analyses were performed to identify the modality of cell death. Monocytes, particularly upon activation, were ore efficient in incorporating sterically stabilized liposomes than all other cells except PMNs. Twenty percent of resting monocytes and up to 65% of activated monocytes died within 24 h of exposure to clodronate-liposomes, whereas the other cell types, including PMNs, remained unaffected. Activated monocytes exposed to clodronate-liposomes, but not resting or activated monocytes exposed to drug-free liposomes, showed clear signs of apoptotic cell death. In most of the assays, sterically stabilized liposomes were more efficient than conventional phosphatidylcholine-liposomes. Sterically stabilized clodronate-liposomes preferentially affect cells of the m.PHI. lineage, particularly if activated. Selective elimination of activated M.PHI.s by apoptosis may explain both therapeutic efficacy and safety of clodronate-liposomes in exptl. models of **autoimmunity.**
ST clodronate liposome monocyte apoptosis **autoimmunity**
IT Arthritis
Autoimmune disease
Macrophage
Monocyte
(apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes)
IT Inflammation inhibitors
(antiarthritics, apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes)
IT Pharmaceutical dosage forms
(liposomes, apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes)
IT **10596-23-3**, Clodronic acid
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes)
IT **10596-23-3**, Clodronic acid
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes)
RN 10596-23-3 HCAPLUS
CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 21 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:162133 HCAPLUS
DN 124:250876
TI Effects of HEBP on experimental osteoporosis in ovariectomized rats and streptozotocin-induced diabetic rats
AU Shibata, Hiroyoshi
CS School Dentistry, Aichi-Gakuin University, Japan
SO Aichi Gakuin Daigaku Shigakkaishi (**1995**), 33(4), 795-811
CODEN: AGDSAB; ISSN: 0044-6912
DT Journal
LA Japanese
CC **1-12** (Pharmacology)
AB Effects of long term administrations of HEBP (1-hydroxyethylidene-1,1-bisphosphonate) at a dose of 0, 2, 4 or 8 mg/kg, every other day on osteoporosis in ovariectomied (OVX) rats, model of high turnover osteoporosis and streptozotocin-induced diabetic (STZD) rats, model of low turnover osteoporosis were examd. OVX rats and STZD rats were administered HEBP for 3 and 2 mo, resp. Tibia, femur and incisor dentin were investigated by chem. analyses and contact microradiog. (CMR). In both OVX and STZD rats, bone loss was obsd. in ash content per unit bone vol. and in CMR of proximal tibia. The bone loss in OVX rats was improved by HEBP at a dose of 2 mg/kg and was partially improved at 4 mg/kg. At a dose of 8 mg/kg, however, HEBP did not improve the bone loss but, rather, potentiated it. In STZD rats, HEBP at a dose of 8 mg/kg increased bone d. At doses of 2 and 4 mg/kg, HEBP had no significant effect on bone loss in STZD rats. These findings indicated that HEBP, well known to inhibit bone resorption as well as mineralization of hard tissues, had a greater effect on bone in OVX rats than STZD rats. Dentin mineralization was not influenced by ovariectomy or streptozotocin treatment. Furthermore, the mineralization in OVX and STZD rats was inhibited dose-dependently to the same degree. Thus, there was no difference in the effect of HEBP on the mineralization in incisor dentin between OVX rats and STZD rats. These results indicated that the effect of HEBP on bone loss was greater in high turnover osteoporosis than in low turnover osteoporosis, and this effect may be based upon the osteoblastic activity in both groups of exptl. animals.
ST osteoporosis hydroxyethylidene bisphosphonate
IT **Diabetes mellitus**
Osteoporosis
(effects of HEBP on exptl. osteoporosis in ovariectomized rats and **diabetic** rats)
IT **2809-21-4**
RL: BAC (Biological activity or effector, except adverse); **THU** **(Therapeutic use)**; BIOL (Biological study); USES (Uses)
(effects of HEBP on exptl. osteoporosis in ovariectomized rats and diabetic rats)
IT **2809-21-4**
RL: BAC (Biological activity or effector, except adverse); **THU** **(Therapeutic use)**; BIOL (Biological study); USES (Uses)
(effects of HEBP on exptl. osteoporosis in ovariectomized rats and diabetic rats)
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



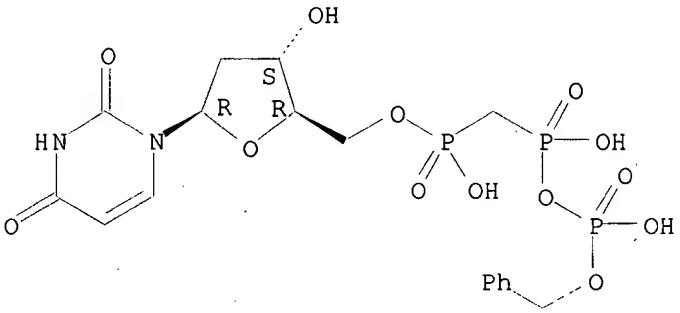
L137 ANSWER 22 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:926080 HCAPLUS
DN 123:330037
TI Agents for inhibiting DNA biosynthesis with improved membrane-permeating properties
IN Zeppezauer, Michael; Nyman, Per Olaf; Zalud, Petra; Wachs, Wolfgang Oliver
PA Germany
SO Ger. Offen., 20 pp.
CODEN: GWXXBX
DT Patent
LA German
IC ICM C07H019-10
ICS A61K031-70
CC **1-12** (Pharmacology)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 4341161	A1	19950608	DE 1993-4341161	19931202 <--
WO 9515332	A1	19950608	WO 1994-EP3969	19941130 <--

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRAI DE 1993-4341161 19931202 <--
AB DUTP analogs which interact with dUTPase similarly to dUTP and disrupt DNA biosynthesis are claimed. Preferred are dUTP analogs in which the O between the .alpha.- and .beta.-phosphate group has been replaced by CH2, NH, or S. 2'-Deoxyuridine-5'-.alpha.,.beta.-methylenetriphosphate monobenzyl ester inhibited OH 77 and EG 463 cell growth at 10 .mu.g/mL.
ST deoxyuridine triphosphate analog DNA biosynthesis inhibitor; cytotoxicity deoxyuridine triphosphate analog; cell proliferation inhibitor deoxyuridine triphosphate analog
IT Neoplasm inhibitors
Virucides and Virustats
(deoxyuridine triphosphate analogs as DNA biosynthesis inhibitors)
IT Deoxyribonucleic acids
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(deoxyuridine triphosphate analogs as DNA biosynthesis inhibitors)
IT **Autoimmune disease**
(inhibitors; deoxyuridine triphosphate analogs as DNA biosynthesis inhibitors)
IT **170428-83-8 170428-84-9** 170428-85-0 170428-86-1
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(deoxyuridine triphosphate analogs as DNA biosynthesis inhibitors)
IT 1173-82-6, Deoxyuridine triphosphate
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(deoxyuridine triphosphate analogs as DNA biosynthesis inhibitors)
IT 37289-34-2, Deoxyuridine triphosphatase
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; deoxyuridine triphosphate analogs as DNA biosynthesis inhibitors)
IT **170428-83-8**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(deoxyuridine triphosphate analogs as DNA biosynthesis inhibitors)

RN 170428-83-8 HCAPLUS
CN Uridine, 2'-deoxy-, 5'-[hydrogen (2,4-dihydroxy-2,4-dioxido-6-phenyl-3,5-dioxa-2,4-diphosphahex-1-yl)phosphonate] (9CI) (CA INDEX NAME)

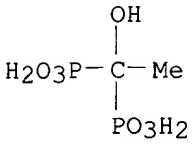
Absolute stereochemistry.



L137 ANSWER 23 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:781303 HCAPLUS
TI Left ventricular hemodynamic parameters in the course of acute experimental coxsackievirus B 3 **myocarditis**
AU Herzum, Matthias; Weller, Rita; **Jomaa, Hassan**; Wietrzychowski, Frank; Pankuweit, Sabine; Mahr, Peter; Maisch, Bernhard
CS Division of Cardiology, Philipps Univ., Marburg, 35043, Germany
SO J. Mol. Cell. Cardiol. (1995), 27(8), 1573-80
CODEN: JMCDAY; ISSN: 0022-2828
PB Academic
DT Journal
LA English
AB In susceptible DBA/2 mice coxsackievirus B 3-induced **myocarditis** leads to inflammatory and necrotic lesions in the myocardium 7-10 days after virus inoculation. The purpose of this study was to det. whether hemodynamic changes occur in murine coxsackievirus B 3 **myocarditis** and whether they are correlated to histol. cardiac lesions throughout the infection. Left ventricular function was detd. by open chest puncture of the left ventricle in the course of acute coxsackievirus B 3 infection. Histol. cross sections of the heart were stained with hematoxylin/eosin and scored blindly for **myocarditic** lesions. Left ventricular function was preserved until day 7 post-virus inoculation. Left ventricular systolic pressure, +dP/dtmax and -dP/dtmax and heart rate declined significantly from day 7 to day 10. The decrease in these parameters did not correlate with viral concns. in the heart on the day of hemodynamic measurements. The decrease was related to histol. changes on day 10, but not on day 7 of the infection. The data suggest (a) that a cumulative loss of cardiac myofibers, induced either by the virus and/or by immune reactions to the heart, is likely to lead to a late depression of cardiac function, and (b) that there is a weak and only temporary structure-function relationship in the heart in coxsackievirus B 3 **myocarditis**. Therefore, in addn. to an anal. of histol. changes, the measurement of cardiac function appears to be very important in order to completely evaluate the severity of **myocarditis** and the usefulness of any therapyl.

L137 ANSWER 24 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:206849 HCAPLUS
DN 122:196796
TI Growth inhibition of macrophage-like and other cell types by liposome-encapsulated, calcium-bound, and free bisphosphonates in vitro
AU Monkkonen, Jukka; Taskinen, Markku; Auriola, Seppo O. K.; Urtti, Arto
CS Dep. Pharmaceutical Technology and A. I. Virtanen Inst., Univ. Kuopio, Kuopio, FIN-70211, Finland
SO J. Drug Targeting (**1994**), 2(4), 299-308
CODEN: JDTAEH; ISSN: 1061-186X

DT Journal
LA English
CC **63-6** (Pharmaceuticals)
Section cross-reference(s): **1**
AB Bisphosphonates effectively inhibit osteoclastic bone resorption in diseases characterized by excessive bone loss. Liposome-encapsulated clodronate (dichloromethylene bisphosphonate) also is known to inactivate phagocytic cells in vivo, and inhibit the growth of macrophage-like RAW 264 cells in vitro. The macrophage suppressive effect of liposomal clodronate is of interest in **autoimmune** disease, like rheumatoid arthritis, in which phagocytic cells are involved in inflammatory processes. Earlier in vivo studies suggested that liposomal clodronate is a far more potent inactivator of macrophages than liposomal forms of two other bisphosphonate compds., pamidronate (3-amino-1-hydroxypropylidene bisphosphonate), and etidronate (1-hydroxyethylidene-1,1-bisphosphonate). The authors examd. the growth inhibitory properties of these three bisphosphonates encapsulated in liposomes effectively inhibited the growth of RAW 264 and CV1-P cells, while free drugs were 20-1000 times less potent growth inhibitors. Also, high extracellular calcium concns. enhanced the potency of bisphosphonates for RAW 264 cells, indicating that, in addn. to liposomes, the uptake of bisphosphonates by macrophages is mediated also by calcium. In all formulations, pamidronate was the most potent compd. for the cells, with the exception of CV1-P cells, for which liposomal clodronate was the most potent. The effects of liposomal drugs were selective for highly endocytotic cells. The results suggest that liposome-encapsulated bisphosphonates could provide a specific tool to affect the function of macrophages and all three of these bisphosphonates are potentially effective as macrophage suppressors in **autoimmune** diseases.
ST macrophage suppressor liposome encapsulated bisphosphonate calcium
IT **Autoimmune disease**
Liposome
Macrophage
(growth inhibition of macrophage-like and other cell types by liposome-encapsulated, calcium-bound, and free bisphosphonates in vitro)
IT Pharmaceutical dosage forms
(liposomes, growth inhibition of macrophage-like and other cell types by liposome-encapsulated, calcium-bound, and free bisphosphonates in vitro)
IT **2809-21-4 10596-23-3 40391-99-9**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(growth inhibition of macrophage-like and other cell types by liposome-encapsulated, calcium-bound, and free bisphosphonates in vitro)
IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(growth inhibition of macrophage-like and other cell types by liposome-encapsulated, calcium-bound, and free bisphosphonates in vitro)
IT 4537-78-4, Distearoylphosphatidylglycerol
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(growth inhibition of macrophage-like and other cell types by liposome-encapsulated, calcium-bound, and free bisphosphonates in vitro)
IT **2809-21-4**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(growth inhibition of macrophage-like and other cell types by liposome-encapsulated, calcium-bound, and free bisphosphonates in vitro)
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

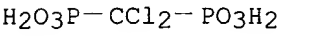


L137 ANSWER 25 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1994:208165 HCAPLUS
DN 120:208165
TI Clodronate (dichloromethylene bisphosphonate) inhibits LPS-stimulated IL-6 and TNF production by raw 264 cells
AU Monkkonen, Jukka; Pennanen, Niina; Lapinjoki, Seppo; Urtti, Arto
CS A. I. Virtanen Inst., Univ. Kuopio, Kuopio, FIN-70211, Finland
SO Life Sci. (**1994**), 54(14), PL229-PL234
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
CC **1-7** (Pharmacology)
Section cross-reference(s): **63**
AB The effect of liposome-encapsulated and free clodronate on the IL-6 and TNF prodn. by macrophages was studied using RAW 264 cell line as a macrophage model, and dissocn.-enhanced lanthanide fluoroimmunoassay (DELFIA) for anal. of secreted cytokines. LPS (lipopolysaccharide)-stimulated RAW 264 cells proved to produce notable amts. of these two cytokines, and DELFIA was sensitive and reliable method for anal. Liposome-encapsulated clodronate inhibited the prodn. of both cytokines, IL-6 being affected more than TNF, and the effect was mostly due to the drug itself, not to liposomal lipid. More than ten times higher concn. of free clodronate than liposomal clodronate was needed to inhibit cytokine prodn. This is the first report on the cytokine inhibitory property of clodronate, and the results support the idea of the use of liposomal clodronate as a macrophage suppressive agent in **autoimmune** diseases.
ST clodronate interleukin tumor necrosis factor macrophage; interleukin 6 macrophage clodronate
IT Immunosuppressants
(clodronate inhibition of interleukin 6 and tumor necrosis factor in macrophages in relation to)
IT Macrophage
(interleukin 6 and tumor necrosis factor formation stimulation by lipopolysaccharides in, free and liposome-encapsulated clodronate inhibition of)
IT Lipopolysaccharides
RL: BIOL (Biological study)
(interleukin 6 and tumor necrosis factor formation stimulation by, in macrophages, free and liposome-encapsulated clodronate inhibition of)
IT Lymphokines and Cytokines
RL: FORM (Formation, nonpreparative)
(interleukin 6, formation of, by macrophages, free and liposome-encapsulated clodronate inhibition of lipopolysaccharide-stimulated)
IT Pharmaceutical dosage forms
(liposomes, for clodronate, interleukin 6 and tumor necrosis factor stimulated by lipopolysaccharides in macrophages inhibition by)
IT Lymphokines and Cytokines
RL: FORM (Formation, nonpreparative)
(tumor necrosis factor, formation of, by macrophages, free and liposome-encapsulated clodronate inhibition of lipopolysaccharide-stimulated)
IT **10596-23-3**, Clodronate
RL: BIOL (Biological study)
(interleukin 6 and tumor necrosis factor stimulated by lipopolysaccharides in macrophages inhibition by free and

liposome-encapsulated)
IT **10596-23-3**, Clodronate
RL: BIOL (Biological study)
(interleukin 6 and tumor necrosis factor stimulated by lipopolysaccharides in macrophages inhibition by free and liposome-encapsulated)
RN 10596-23-3 HCAPLUS
CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)

L137 ANSWER 26 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1994:153244 HCAPLUS
DN 120:153244
TI Selective elimination of macrophages by dichlormethylene diphosphonate-containing liposomes suppresses experimental **autoimmune** neuritis
AU Jung, Stefan; Huitinga, Ingeborg; Schmidt, Beate; Zielasek, Juergen; Dijkstra, Christine D.; Toyka, Klaus V.; Hartung, Hans Peter
CS Dep. Neurol., Julius-Maximilians-Univ., Wurzburg, Germany
SO J. Neurol. Sci. (**1993**), 119(2), 195-202
CODEN: JNSCAG; ISSN: 0022-510X
DT Journal
LA English
CC **1-7** (Pharmacology)
AB The injection of liposome-encapsulated dichlormethylene diphosphonate (Cl2MDP) constitutes an effective method to selectively eliminate phagocytic cells from spleen, liver and the circulation. The authors evaluated the effect of Cl2MDP-liposomes on the course of actively induced and adoptively transferred exptl. **autoimmune** neuritis (EAN), both animal models of the human Guillain-Barre syndrome. Injection of Cl2MDP-liposomes 11 and 13 days post-immunization (p.i.) of Lewis rats with bovine peripheral nerve myelin efficiently prevented clin. signs of EAN up to day 15 p.i., when all control animals were affected. Thereafter, EAN gradually also developed in Cl2MDP-liposome-treated rats, but until day 19, disease was significantly milder than in control rats injected with buffer-filled liposomes. Adoptive transfer EAN (AT-EAN) induced by injection of activated P2-specific T cells could be suppressed even more markedly by application of Cl2MDP-liposomes 1, 3, and 6 days after cell transfer. Efficient suppression of AT-EAN by Cl2MDP-liposomes rules out the possibility that EAN is prevented due to interference with the induction phase of this exptl. disease and confirms that macrophages are important effector cells during EAN. Selective suppression of phagocytic cell function by drug-contg. liposomes may hold promise as a novel treatment of demyelinating **autoimmune** diseases of the nervous system.
ST dichlormethylene diphosphonate liposome **autoimmune** neuritis macrophage
IT Macrophage
(**autoimmune** neuritis treatment with dichlormethylene diphosphonate-contg. liposomes in relation to inhibition of)
IT Nervous system
(disease, Guillain-Barre syndrome, dichlormethylene diphosphonate-contg. liposomes for treatment of, macrophages inhibition in relation to)
IT Pharmaceutical dosage forms
(liposomes, dichlormethylene diphosphonate-contg., **autoimmune** neuritis treatment with, macrophages inhibition in)
IT Nerve, disease
(neuritis, **autoimmune**, dichlormethylene diphosphonate-contg. liposomes treatment of, macrophages inhibition in relation to)
IT **10596-23-3**
RL: BIOL (Biological study)

(liposomes contg., **autoimmune** neuritis treatment with, macrophages inhibition in)
IT **10596-23-3**
RL: BIOL (Biological study)
(liposomes contg., **autoimmune** neuritis treatment with, macrophages inhibition in)
RN 10596-23-3 HCAPLUS
CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 27 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1994:124843 HCAPLUS
DN 120:124843
TI The effects of liposome-encapsulated and free clodronate on the growth of macrophage-like cells in vitro: the role of calcium and iron
AU Monkkonen, Jukka; Heath, Timothy D.
CS Sch. Pharm., Univ. Wisconsin, Madison, WI, 53706, USA
SO Calcif. Tissue Int. (**1993**), 53(2), 139-46
CODEN: CTINDZ; ISSN: 0171-967X
DT Journal
LA English
CC **1-12** (Pharmacology)
Section cross-reference(s): **63**
AB Clodronate (dichloromethylene bisphosphonate) inhibits the activity of osteoclasts, thereby preventing bone resorption in disorders characterized by excessive bone loss. I.v. injected clodronate encapsulated in liposomes is also known to inactivate phagocytic cells in spleen and liver in vivo. The macrophage suppressive effect of clodronate is of interest in **autoimmune** diseases, like rheumatoid arthritis, in which phagocytic cells are involved in inflammatory processes, but knowledge of the interaction of clodronate with phagocytic cells is scarce. The authors have studied the uptake of clodronate, both free and encapsulated in neg. charged liposomes, by the macrophage-like cell line RAW 264 and by other types of cell lines. The uptake was assessed by a growth inhibition assay. The liposome-encapsulated clodronate was 50 and 350 times more potent than free drug for RAW 264 and CV1-P, resp. Cell lines with a lower endocytic capacity were insensitive to liposome-mediated delivery of the drug. The action of free clodronate seemed to be extracellular in all cell lines studied. Calcium and/or iron have been suggested to be involved in the intracellular uptake and action of clodronate in phagocytic cells. The authors found that the uptake of free clodronate by RAW 264 cells was indeed mediated by calcium and iron, while the uptake of liposomal drugs was only slightly affected by calcium. The increased intracellular calcium concn. in macrophages did not significantly affect the growth-inhibitory properties of clodronate, whereas iron loading of the cells partially restored the cell growth. The data do not support the role of calcium chelation as a mechanism of action of clodronate, but suggest that intracellular iron is, at least partially involved.
ST liposome encapsulated clodronate macrophage calcium iron
IT Macrophage
(growth of, liposome-encapsulated clodronate inhibition of, uptake in, calcium and iron in)
IT Cell proliferation
(of macrophage, liposome-encapsulated clodronate inhibition of, uptake in, calcium and iron in)
IT Biological transport
(absorption, of liposome-encapsulated clodronate, by macrophage, calcium and iron in)
IT Pharmaceutical dosage forms
(liposomes, for clodronate, macrophage growth inhibition by and uptake of, calcium and iron in)
IT 7439-89-6, Iron, biological studies 7440-70-2, Calcium, biological

studies
RL: BIOL (Biological study)
(in macrophage growth inhibition and uptake of liposome-encapsulated clodronate)
IT **10596-23-3**, Clodronate
RL: BIOL (Biological study)
(macrophage growth inhibition by and uptake of, liposome encapsulation effect on, calcium and iron in)
IT **10596-23-3**, Clodronate
RL: BIOL (Biological study)
(macrophage growth inhibition by and uptake of, liposome encapsulation effect on, calcium and iron in)
RN 10596-23-3 HCAPLUS
CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)

$H_2O_3P-CCl_2-PO_3H_2$

L137 ANSWER 28 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1994:8745 HCAPLUS
DN 120:8745
TI Preparation of methanediphosphonic acid derivatives as drugs
IN Kawabe, Norio; Uchiro, Hiromi; Nakadate, Teruo; Tanahashi, Masahiko; Ito, Masatoshi
PA Toray Industries, Inc., Japan
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM C07F009-38
ICS C07F009-40; A61K031-66
CC 29-7 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9305052	A1	19930318	WO 1992-JP1140	19920907	<--
	W: CA, JP, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE					
	EP 594857	A1	19940504	EP 1992-918702	19920907	<--
	EP 594857	B1	19980429			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE					
	JP 08026048	B4	19960313	JP 1992-504234	19920907	<--
	CA 2095128	C	19980106	CA 1992-2095128	19920907	<--
	AT 165603	E	19980515	AT 1992-918702	19920907	<--
	ES 2114946	T3	19980616	ES 1992-918702	19920907	<--
	US 5527940	A	19960618	US 1994-340819	19941117	<--
	US 5683992	A	19971104	US 1996-617937	19960315	<--
PRAI	JP 1991-226175	19910905	<--			
	JP 1992-179802	19920707	<--			
	WO 1992-JP1140	19920907	<--			
	US 1993-50084	19930428	<--			
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OS MARPAT 120:8745
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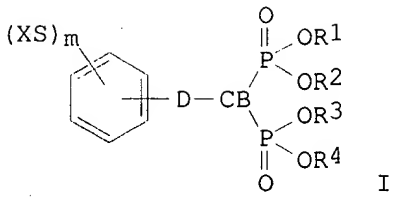

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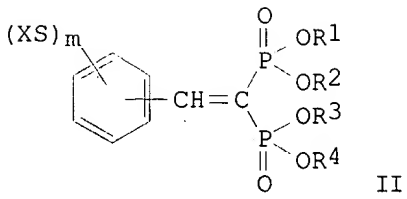


II

AB The title compds. [I and II; B = H, alkyl, OH, alkoxy, NH2; D = O, S, (alkyl)imino, OH2, SCH2; x = (hetero-substituted) alkyl, aryl, acyl; R1-R4 = H, C1-7 alkyl; m = 1-5], effective in treating inflammation, rheumatism, bone metab. disorders, osteoporosis, **autoimmune** disease, and useful as interleukin-1 inhibitors and antioxidants, are prepd. Grignard reaction of 4-BrC6H4SMe with Mg in THF and subsequent refluxing with cryst. S gave 72% (4-MeSC6H4)2S2, which was treated with a reaction mixt. of CH2[P(O)(OEt)2]2 and BuLi in THF-hexane to give 41% p-I (R1-R4 = Et, B = H, D = S, X = Me, m = 1) (III). Treating III with BrSiMe3 in CH2Cl2 under Ar gave 69% p-I (R1-R4 = H, others remain unchanged as in III), which showed antiinflammatory activity at 20 mg/kg in rats, 62.3% inhibition of bone destruction, 51.1% inhibition of interleukin-1 formation, 46.3 .+-. 0.81% inhibition of active O formation, and 79.9 .+-. 3.12% inhibition of bone resorption.

ST methanediphosphonate prepn drug; interleukin 1 inhibitor methanediphosphonate prepn; antioxidant methanediphosphonate prepn; bone resorption inhibitor methanediphosphonate prepn; antiinflammatory methanediphosphonate prepn; antirheumatic methanediphosphonate prepn; **autoimmune** disease methanediphosphonate prepn

IT Antioxidants
Inflammation inhibitors
(methanediphosphonic acid derivs.)

IT **Autoimmune disease**
Osteoporosis
(treatment of, methanediphosphonic acid derivs. for)

IT Lymphokines and Cytokines
RL: USES (Uses)
(interleukin 1, inhibitors, metanediphosphonic acid derivs.)

IT Bone, disease
(metabolic, treatment of, methanediphosphonic acid derivs. for)

IT 7704-34-9, Sulfur, reactions
RL: RCT (Reactant)
(Grignard reaction of, in prepn. of drugs)

IT 104-95-0, 4-Bromothioanisole
RL: RCT (Reactant)
(Grignard reaction of, with sulfur, in prepn. of drugs)

IT **151425-90-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrolysis of, in prepn. of drugs)

IT 59014-88-9P 84910-80-5P 93972-94-2P 151426-21-0P 151426-22-1P 151426-23-2P 151426-24-3P 151426-25-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of drug)

IT 20057-77-6P, Bis[4-(methylthio)phenyl] disulfide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of drugs)

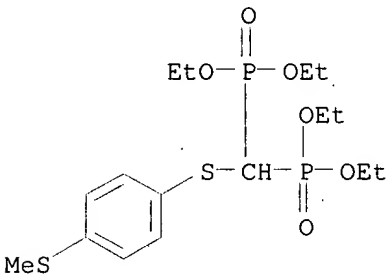
IT **151425-91-1P 151425-92-2P 151425-93-3P**
151425-94-4P 151425-95-5P 151425-96-6P
151425-97-7P 151425-98-8P 151425-99-9P
151426-00-5P 151426-01-6P 151426-02-7P
151426-03-8P 151426-04-9P 151426-05-0P
151426-06-1P 151426-07-2P 151426-08-3P
151426-09-4P 151426-10-7P 151426-11-8P
151426-12-9P 151426-13-0P 151426-14-1P
151426-15-2P 151426-16-3P 151426-17-4P

151426-18-5P 151426-19-6P 151426-20-9P
151456-40-5P 151456-41-6P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as drug)

IT **1660-94-2**, Tetraethyl methylenediphosphonate
RL: RCT (Reactant)
(reaction of, with bis(methylthiophenyl) disulfide in prepn. of drugs)

IT **151425-90-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**
(prepn. and hydrolysis of, in prepn. of drugs)

RN 151425-90-0 HCAPLUS
CN Phosphonic acid, [[[4-(methylthio)phenyl]thio]methylene]bis-, tetraethyl ester (9CI) (CA INDEX NAME)



L137 ANSWER 29 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1990:491460 HCAPLUS
DN 113:91460
TI Substituted adenine derivatives useful as therapeutic agents
IN Carson, Dennis A.; Carrera, Carlos J.
PA Scripps Clinic and Research Foundation, USA
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07H019-19
ICS A61K031-70
CC **1-7** (Pharmacology)
Section cross-reference(s): 33, **63**

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8908658	A1	19890921	WO 1989-US1088	19890316 <--
	W: AU, DK, FI, JP, KR, NO				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	AU 8934105	A1	19891005	AU 1989-34105	19890316 <--
	AU 626296	B2	19920730		
	EP 364559	A1	19900425	EP 1989-904431	19890316 <--
	EP 364559	B1	19950920		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 03501258	T2	19910322	JP 1989-504299	19890316 <--
	JP 3090456	B2	20000918		
	AT 128141	E	19951015	AT 1989-904431	19890316 <--
	CA 1339964	A1	19980721	CA 1989-593979	19890316 <--
	DK 8905721	A	19891115	DK 1989-5721	19891115 <--
	DK 170629	B1	19951120		
	NO 8904558	A	19891115	NO 1989-4558	19891115 <--
	CA 2191230	AA	19951207	CA 1994-2191230	19940526 <--
	AU 9474707	A1	19951221	AU 1994-74707	19940526 <--
	JP 10505323	T2	19980526	JP 1994-500782	19940526 <--

AU 9918593 A1 19990506 AU 1999-18593 19990304 <--
PRAI US 1988-169618 19880316 <--
US 1989-323350 19890314 <--
WO 1989-US1088 19890316 <--
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WO 1994-US5971 19940526 <--
OS MARPAT 113:91460
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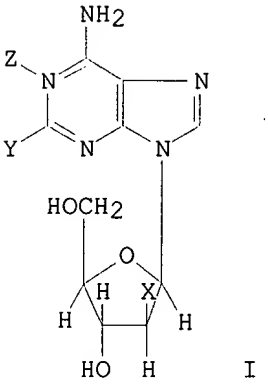


I

AB Substituted adenine derivs. I (e.g. Z = O or absent; Y = H or a substituent contg. 1-20 atoms that is free from net ionic charge at physiol. pH values; X = H or F; when Z is absent, X = F; Y is H only when Z is present and X = F) are effective in treating **autoimmune** diseases and monocyte-mediated disorders. For treating monocyte-mediated diseases, an antimicrobial agent in addn. to I may be administered. EDs of I for treating monocyte-mediated disease, **autoimmune** disease (i.e. rheumatoid arthritis), and AIDS are claimed. No therapeutic tests are given. In vitro as well as in vivo cytotoxicity of 2-chlorodeoxyadenosine is described. Thus, 2-chloro-9,1'-.beta.-2'-deoxy-2'-fluoro-D-arabinofuranosyl adenine (II) was prepd. starting from 1,3'-di-O-acetyl-5'-O-benzoyl-2'-deoxy-2'-fluoro-.beta.-D-arabinose via 3'-O-acetyl-5'-O-benzoyl-2'-deoxy-2-fluoro-D-arabinofuranosyl bromide and 2,6'-dichloro-9,1'-(3'-O-acetyl-5-O-benzoyl-2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-9-purine. Tablets were prepd. contg. II 1, starch 40, modified starch 10, Mg stearate 1-5 mg and CaHPO4 q.s.

ST adenine deriv pharmaceutical **autoimmune** disease; monocyte mediated disease adenine deriv; AIDS pharmaceutical adenine deriv

IT Interferons
RL: BIOL (Biological study)
(AIDS treatment with 2-chloro-2'-deoxyadenosine and)

IT Phagocytosis
Ribonucleic acid formation
(by monocyte after exposure to chlorodeoxyadenosine)

IT Immunosuppression
(by substituted adenine derivs.)

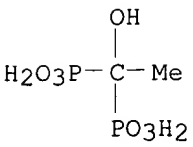
IT Fibroblast
Lymphocyte
Monocyte
Neutrophil
(chlorodeoxyadenosine cytotoxicity to)

IT Deoxyribonucleic acids
RL: BIOL (Biological study)
(damage to, in monocytes after exposure to chlorodeoxyadenosine)

IT Disease
(monocyte-mediated, treatment of, substituted adenine derivs. for)

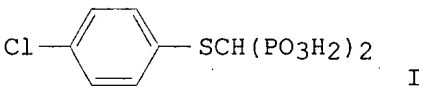
IT Pharmaceutical dosage forms

(substituted adenine deriv.-contg., for treating **autoimmune** diseases and monocyte-mediated diseases)
IT Immunodeficiency
(acquired immune deficiency syndrome, treatment of, substituted adenine derivs. for)
IT Inflammation inhibitors
(antiarthritics, substituted adenine derivs. as)
IT Disease
(**autoimmune**, treatment of, substituted adenine derivs. for)
IT Bactericides, Disinfectants, and Antiseptics
Virucides and Virustats
(medical, monocyte-mediated disease treatment with substituted adenine derivs. and)
IT Interferons
RL: PROC (Process)
(.beta.2, release of, by monocyte after exposure to chlorodeoxyadenosine)
IT 7481-89-2, 2',3'-Dideoxycytidine 30516-87-1 59277-89-3, Acyclovir
RL: BIOL (Biological study)
(AIDS treatment with 2-chloro-2'-deoxyadenosine and)
IT 4291-63-8, 2-Chloro-2'-deoxyadenosine
RL: BIOL (Biological study)
(AIDS treatment with azidothymidine and)
IT 53-03-2, Prednisone 54-05-7, Chloroquine 58-14-0, Pyrimethamine 63-74-1 90-34-6, Primaquine 100-33-4 107-36-8 599-79-1, Sulfasalazine 1397-89-3, Amphotericin B **7414-83-7** 8064-90-2 16037-91-5 23256-30-6, Nifurtimox 53230-10-7, Mefloquine 128994-33-2
RL: BIOL (Biological study)
(monocyte-mediated disease treatment with substituted adenine derivs. and)
IT 53-84-9, NAD 56-65-5, ATP, biological studies
RL: BIOL (Biological study)
(of monocytes after exposure to chlorodeoxyadenosine)
IT 4291-63-8 123318-82-1 128994-34-3
RL: BIOL (Biological study)
(pharmaceuticals contg., for treating **autoimmune** and monocyte-mediated diseases)
IT 56632-81-6P 103884-99-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, for therapeutic adenine deriv. prepn.)
IT 3506-01-2P 123318-82-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for treating **autoimmune** or monocyte-mediated diseasesmonocyte-mediated disease)
IT 56632-80-5
RL: RCT (Reactant)
(reaction of, for therapeutic adenine deriv. prepn.)
IT 958-09-8, 2'-Deoxyadenosine
RL: RCT (Reactant)
(reaction of, for therapeutic deoxyadenosine oxide prepn.)
IT 5451-40-1, 2,6-Dichloropurine
RL: RCT (Reactant)
(reaction of, with acetylbenzoyldeoxyfluoroarabinofurosyl bromide)
IT **7414-83-7**
RL: BIOL (Biological study)
(monocyte-mediated disease treatment with substituted adenine derivs. and)
RN 7414-83-7 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



● 2 Na

L137 ANSWER 30 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1987:60920 HCAPLUS
DN 106:60920
TI Effect of (4-chlorophenyl)thiomethylenebisphosphonic acid (SR 41319) on the **autoimmune** disease activity in MRL/l mice
AU Barbier, A.; Planchenault, C.; Breliere, J. C.
CS Clin-Midy Res. Cent., Sanofi Res., Montpellier, 34082, Fr.
SO Agents Actions (**1986**), 19(5-6), 311-12
CODEN: AGACBH; ISSN: 0065-4299
DT Journal
LA English
CC **1-7** (Pharmacology)
GI



I

AB MRL-lpr/lpr (MRL/1) mice spontaneously develop an **autoimmune** pathol. including arthritic lesions. SR 41319 (I) [**96538-83-9**], a bisphosphonate, having previously shown to be active in in vitro and in vivo models of arthritis, was studied for its possible effect on the pathol. of the disease in MRL/1 mice. Results showed that SR 41319 reduced the severity of the disease in its early stages and increased mean life span.
ST **autoimmune** disease chlorophenylthiomethylenebisphosphonate; SR 41319 **autoimmune** disease
IT Disease
(**autoimmune**, inhibition of, by (chlorophenyl)thiomethylenebis phosphonic acid)
IT **96538-83-9**, SR 41319
RL: BIOL (Biological study)
(**autoimmune** disease inhibition by)
IT **96538-83-9**, SR 41319
RL: BIOL (Biological study)
(**autoimmune** disease inhibition by)
RN 96538-83-9 HCAPLUS

L137 ANSWER 31 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1985:404838 HCAPLUS
DN 103:4838
TI Comparative study of etidronate and SR 41319, a new diphosphonate, on passive cutaneous anaphylaxis and phospholipase A2 activity
AU Barbier, A.; Breliere, J. C.; Paul, R.; Roncucci, R.
CS Cent. Rech. CLIN-MIDY, SANOFI, Montpellier, 34082, Fr.
SO Agents Actions (**1985**), 16(1-2), 41-2
CODEN: AGACBH; ISSN: 0065-4299
DT Journal
LA English
CC **15-9** (Immunochemistry)

Section cross-reference(s): **1**

AB Diphosphonates are known to affect Ca metab. It was therefore of interest to investigate the effects of SR 41319, a new diphosphonate, in comparison with etidronate disodium (EHDP) on passive cutaneous anaphylaxis (PCA) and on phospholipase A2 (PLA2) activity which are both mediated by Ca-dependent mechanisms. Results showed that: (1) i.v., SR 41319 induced a dose-dependent inhibition of PCA more pronounced than that of EHDP; (2) in PLA2 assay, marked inhibition was obtained with SR 41319, whereas EHDP was slightly active. Decrease in Ca entry into mast cells and anti-PLA2 activity of SR 41319 might partly explain the SR 41319 inhibition of PCA.

ST anaphylaxis phospholipase SR41319 diphosphonate; hypersensitivity treatment SR41319 diphosphonate

IT Mast cell
(passive cutaneous anaphylaxis and phospholipase A2 of, SR 41319 diphosphonate effect on)

IT **Allergy**
(hypersensitivity, treatment of, SR 41319 diphosphonate effects on passive cutaneous anaphylaxis and phospholipase A2 of mast cell in relation to)

IT Anaphylaxis
(passive cutaneous, SR 41319 diphosphonate effect on, of mast cell)

IT 7440-70-2, biological studies
RL: BIOL (Biological study)
(SR 41319 diphosphonate effects on passive cutaneous anaphylaxis and phospholipase A2 of mast cell in relation to)

IT 9001-84-7
RL: BIOL (Biological study)
(of mast cell, SR 41319 effect on)

IT **96538-83-9**
RL: BIOL (Biological study)
(passive cutaneous anaphylaxis and phospholipase A2 of mast cell response to)

IT **96538-83-9**
RL: BIOL (Biological study)
(passive cutaneous anaphylaxis and phospholipase A2 of mast cell response to)

RN 96538-83-9 HCAPLUS

L137 ANSWER 32 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1979:413944 HCAPLUS

DN 91:13944

TI Effect of the diphosphonate EHDP on plasma inorganic phosphate and hemoglobin oxygen affinity of diabetic and healthy subjects

AU Ditzel, Joern; Hau, C.; Daugaard, Niels

CS Dep. Med., Aalborg Reg. Hosp., Aalborg, Den.

SO Adv. Exp. Med. Biol. (**1977**), 81(Phosphate Metab.), 423-30
CODEN: AEMBAP; ISSN: 0065-2598

DT Journal

LA English

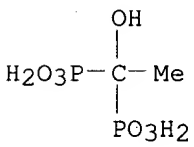
CC **1-6** (Pharmacodynamics)
Section cross-reference(s): 14

AB The effect of oral 2Na ethane-1-hydroxy-1,1-diphosphonate (EHDP) [**7414-83-7**] (20 mg/kg daily) and placebo given for 28 days on plasma inorg. phosphate (Pi), red cell 2,3-diphosphoglycerate [7782-44-7], and O affinity of Hb was evaluated in insulin-treated diabetics and healthy volunteers. EHDP significantly increased mean Pi (diabetics: 1.18-1.67 mmol/L, controls: 1.03-1.71 mmol/L, and the O affinity P50 (pO50 at 50% O satn.) at in vivo pH of the oxyHb dissocn. curve (diabetics: 25.4-26.6 mmHg, controls: 26.3-28.9 mmHg). Pi and P50 were correlated in both diabetics and in controls. 2,3-Diphosphoglycerate increased when the diabetics were on EHDP. The study emphasizes the importance of Pi on red cell function and indicates that an elevation of Pi tends to counteract the defect in O release capacity of the red cells in diabetic subjects.

ST diabetes erythrocyte oxygen phosphate; diphosphonate Hb oxygen diabetes

IT Blood plasma

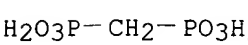
(inorg. phosphate of, in diabetes, diphosphonate effect on, Hb and O affinity in relation to)
IT Erythrocyte
(inorg. phosphate of, in diabetes, oxygen affinity of Hbs in relation to)
IT **Diabetes mellitus**
(oxygen affinity of Hbs in, inorg. phosphate of erythrocyte in relation to)
IT Hemoglobins
RL: PRP (Properties)
(oxygen affinity of, in diabetes, inorg. phosphate of erythrocytes in relation to)
IT 7782-44-7, biological studies
RL: PRP (Properties)
(affinity of, in Hbs in diabetes, inorg. phosphate of erythrocytes in relation to)
IT **7414-83-7**
RL: BIOL (Biological study)
(inorg. phosphate of blood plasma and oxygen affinity of Hbs response to, in diabetes)
IT **7414-83-7**
RL: BIOL (Biological study)
(inorg. phosphate of blood plasma and oxygen affinity of Hbs response to, in diabetes)
RN 7414-83-7 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



● 2 Na

L137 ANSWER 33 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1977:594043 HCAPLUS
DN 87:194043
TI Methylene diphosphonic acid inhibition of the delayed and immediate types of hypersensitivity in guinea pigs
AU Komissarenko, S. V.; Zhuravskii, N. I.; Karlova, N. P.; Gulyi, M. F.
CS A. V. Palladin Inst. Biochem., Kiev, USSR
SO Byull. Eksp. Biol. Med. (**1977**), 84(9), 339-41
CODEN: BEBMAE
DT Journal
LA Russian
CC **1-5** (Pharmacodynamics)
AB Methylene diphosphonic acid [**1984-15-2**] (30 .mu.g/g) injected s.c. into guinea pigs inhibited both immediate and delayed hypersensitivity to sheep red blood cells.
ST methylene diphosphonate hypersensitivity; **allergy** methylene diphosphonate
IT **Allergy**
(delayed hypersensitivity, methylene diphosphonate inhibition of)
IT **Allergy**
(hypersensitivity, methylene diphosphonate inhibition of)
IT **1984-15-2**
RL: BIOL (Biological study)
(**allergy** response to)
IT **1984-15-2**

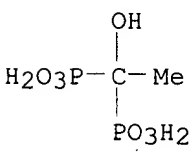
RL: BIOL (Biological study)
(**allergy** response to)
RN 1984-15-2 HCAPLUS
CN Phosphonic acid, methylenebis- (9CI) (CA INDEX NAME)



L137 ANSWER 34 OF 35 HCAPLUS COPYRIGHT 2001 ACS
AN 1977:527290 HCAPLUS
DN 87:127290
TI The effects of various diphosphonates on a rat model of cardiac calciphylaxis
AU Rosenblum, I. Y.; Black, H. E.; Ferrell, J. F.
CS Miami Val. Lab., Procter and Gamble Co., Cincinnati, Ohio, USA
SO Calcif. Tissue Res. (**1977**), 23(2), 151-9
CODEN: CATRBZ
DT Journal
LA English
CC **1-5** (Pharmacodynamics)
Section cross-reference(s): 14
AB Seven diphosphonate analogs were tested for their effects on myocardial and cardiovascular degeneration and calcification in an exptl. model of cardiac calciphylaxis. A single oral dose of dihydrotachysterol (DHT) [67-96-9] administered to rats induced myocardial and vascular degeneration, focal **myocarditis** and vasculitis, and myocardial and vascular mineralization. The results demonstrated a considerable variation among the various diphosphonates in their ability to block the pathol. changes obsd. in this model. Ethane-1-hydroxy-1,1-diphosphonic acid (EHDP) [**2809-21-4**] was the most effective diphosphonate in reducing myocardial and vascular degeneration and calcification, whereas diphosphonates such as ethane-1-amino-1,1-diphosphonic acid (EADP) [**15049-85-1**] and hydroxymethylene diphosphonic acid (HMDP) [**15468-10-7**] had little or no effect compared to saline controls. For those diphosphonates which were effective, e.g., EHDP, the tissue-protective effects were obsd. whether the rats were treated with drug prior to the administration of DHT, or whether drug treatment commenced after DHT administration. The results are discussed in terms of the known biol. properties of the diphosphonate drugs.
ST diphosphonate heart calciphylaxis
IT Calciphylaxis
(of heart, diphosphonates effect on)
IT Heart, disease or disorder
(calciphylaxis, diphosphonate effect on)
IT 67-96-9
RL: BIOL (Biological study)
(heart calciphylaxis from, diphosphonates effect on)
IT **1984-15-2 2809-21-4 10596-23-3**
15049-85-1 15468-10-7 29712-28-5
34393-98-1 36465-90-4D, analogs
RL: BIOL (Biological study)
(heart calciphylaxis response to)
IT **1984-15-2**
RL: BIOL (Biological study)
(heart calciphylaxis response to)
RN 1984-15-2 HCAPLUS
CN Phosphonic acid, methylenebis- (9CI) (CA INDEX NAME)

L137 ANSWER 35 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1977:515854 HCAPLUS
DN 87:115854
TI Effect of the diphosphonate ethane-1-hydroxy-1, 1-diphosphonate (EHDP) on hemoglobin oxygen affinity of diabetic and healthy subjects
AU Ditzel, Joern; Hau, Christian; Daugaard, Niels
CS Dep. Med., Aalborg Reg. Hosp., Aalborg, Den.
SO Microvasc. Res. (**1977**), 13(3), 355-61
CODEN: MIVRA6
DT Journal
LA English
CC 14-3 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 13
AB To study the effect of prolonged elevation of plasma inorganic phosphate (Pi) on red cell metabolism and function, oxyhemoglobin dissocn. curves from zero to full satn. were performed on whole blood from insulin-treated, nonacidotic diabetics and healthy volunteers following oral administration of disodium ethane-1-hydroxy-1,1-diphosphonate (EHDP) (20 mg kg-1 day-1) or placebo for 28 days. EHDP increased mean Pi and pO2 at 50% O2 satn. (P50). P1 and P50 were correlated in both diabetics and controls. Mean P50 in diabetics was lower than normal in spite of normal red cell 2,3-diphosphoglycerate. 2,3-Diphosphoglycerate increased when the diabetics were on EHDP, while no changes occurred in Hb concn., O satn., or blood pH. The study emphasizes the importance of Pi on red cell function and indicates that an elevation of Pi tends to counteract the defect in oxygen-release capacity of the red cells in diabetic subjects.
ST Hb oxygen affinity diabetes; phosphate Hb oxygen affinity
IT **Diabetes mellitus**
(hemoglobin oxygen binding in, phosphate of blood in relation to)
IT Hemoglobins
RL: BIOL (Biological study)
(oxygen binding of, phosphate of blood in relation to)
IT Blood
(phosphate of, hemoglobin oxygen affinity in relation to)
IT 7782-44-7, biological studies
RL: BIOL (Biological study)
(hemoglobin binding of, phosphate of blood in relation to)
IT 14265-44-2, biological studies
RL: BIOL (Biological study)
(of blood, hemoglobin oxygen binding in relation to)
IT **7414-83-7**
RL: BIOL (Biological study)
(phosphate of blood in response to, hemoglobin oxygen affinity in relation to)
IT **7414-83-7**
RL: BIOL (Biological study)
(phosphate of blood in response to, hemoglobin oxygen affinity in relation to)
RN 7414-83-7 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



● 2 Na

=> fil reg

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5	RN	**151456-40-5**	REGISTRY
6	RN	**151426-20-9**	REGISTRY
7	RN	**151426-19-6**	REGISTRY
8	RN	**151426-18-5**	REGISTRY
9	RN	**151426-17-4**	REGISTRY
10	RN	**151426-16-3**	REGISTRY
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21	RN	**151426-05-0**	REGISTRY
22	RN	**151426-04-9**	REGISTRY
23	RN	**151426-03-8**	REGISTRY
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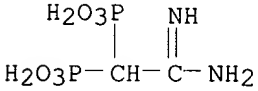
25	RN	**151426-01-6**	REGISTRY
26	RN	**151426-00-5**	REGISTRY
27	RN	**151425-99-9**	REGISTRY
28	RN	**151425-98-8**	REGISTRY
29	RN	**151425-97-7**	REGISTRY
30	RN	**151425-96-6**	REGISTRY
31	RN	**151425-95-5**	REGISTRY
32	RN	**151425-94-4**	REGISTRY
33	RN	**151425-93-3**	REGISTRY
34	RN	**151425-92-2**	REGISTRY
35	RN	**151425-91-1**	REGISTRY
36	RN	**151425-90-0**	REGISTRY
37	RN	**138926-19-9**	REGISTRY
38	RN	**138330-18-4**	REGISTRY
DR	183808-97-1		
39	RN	**129318-43-0**	REGISTRY
40	RN	**124351-85-5**	REGISTRY
41	RN	**121268-17-5**	REGISTRY
42	RN	**118072-93-8**	REGISTRY
43	RN	**114084-78-5**	REGISTRY
44	RN	**105462-24-6**	REGISTRY
45	RN	**105462-23-5**	REGISTRY
46	RN	**89987-06-4**	REGISTRY

DR **96538-83-9**
47 RN **89130-99-4** REGISTRY
48 RN **79778-41-9** REGISTRY
49 RN **66376-36-1** REGISTRY
50 RN **57248-88-1** REGISTRY
51 RN **41003-10-5** REGISTRY
52 RN **40391-99-9** REGISTRY
53 RN **34393-98-1** REGISTRY
54 RN **29712-28-5** REGISTRY
55 RN **15468-10-7** REGISTRY
56 RN **15049-85-1** REGISTRY
57 RN **10596-23-3** REGISTRY
DR 163706-60-3
58 RN **7414-83-7** REGISTRY
DR 187285-10-5
59 RN **7292-42-4** REGISTRY
DR 172664-67-4, 55916-39-7
60 RN **2809-21-4** REGISTRY
DR 129130-42-3, 51888-66-5, 66216-98-6, 85985-26-8, 86159-18-4, 100511-44-2, 106908-76-3
61 RN **1984-15-2** REGISTRY
DR 63347-66-0
62 RN **1660-94-2** REGISTRY

=> d ide can l138 1 2 4 37-62

Samples from hits 1-62, L138

L138 ANSWER 1 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **253265-92-8** REGISTRY
CN Phosphonic acid, (2-amino-2-iminoethylidene)bis- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C2 H8 N2 O6 P2
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

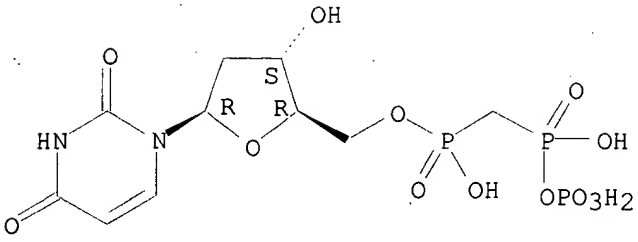


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:59143

L138 ANSWER 2 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **170428-84-9** REGISTRY
CN Uridine, 2'-deoxy-, 5'-[hydrogen [[hydroxy(phosphonooxy)phosphinyl]methyl] phosphonate] (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C10 H17 N2 O13 P3
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

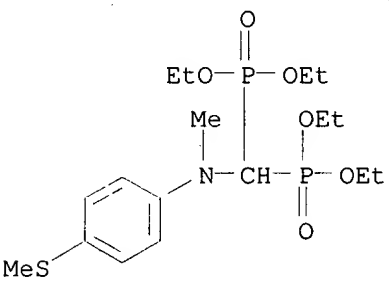
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:330037

L138 ANSWER 4 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **151456-41-6** REGISTRY
CN Phosphonic acid, [[methyl[4-(methylthio)phenyl]amino]methylene]bis-, tetraethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C17 H31 N O6 P2 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:8745

L138 ANSWER 37 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **138926-19-9** REGISTRY
CN Phosphonic acid, [1-hydroxy-3-(methylpentylamino)propylidene]bis-, monosodium salt, monohydrate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN BM 21.0955Na.H2O
CN Ibandronate sodium monohydrate
MF C9 H23 N O7 P2 . H2 O . Na
SR CAS Registry Services
LC STN Files: ADISINSIGHT, BIOTECHNO, CA, CAPLUS, DRUGPAT, DRUGUPDATES, EMBASE, MRCK*, SYNTHLINE, TOXLIT
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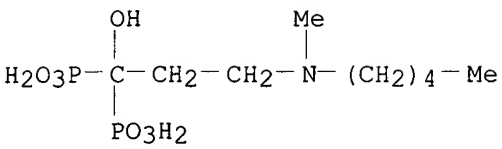

● Na

● H_2O

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:284250

REFERENCE 2: 132:284249

REFERENCE 3: 132:69329

L138 ANSWER 38 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **138330-18-4** REGISTRY
CN Phosphonic acid, [(cycloheptylamino)methylene]bis-, disodium salt (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Incadronate
CN Incadronate disodium
CN YM 175
DR 183808-97-1
MF C8 H19 N O6 P2 . 2 Na
SR CA
LC STN Files: ADISINSIGHT, ANABSTR, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, CIN, DDFU, DRUGPAT, DRUGU, DRUGUPDATES, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, SYNTHLINE, TOXLINE, TOXLIT, USPATFULL
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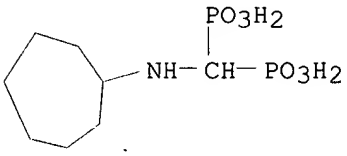

● 2 Na

63 REFERENCES IN FILE CA (1967 TO DATE)
63 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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REFERENCE 2: 134:36866

REFERENCE 3: 133:344627

REFERENCE 4: 133:313639

REFERENCE 5: 133:294826

REFERENCE 6: 133:217722

REFERENCE 7: 133:217721

REFERENCE 8: 133:17634

REFERENCE 9: 132:288773

REFERENCE 10: 132:284250

L138 ANSWER 39 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **129318-43-0** REGISTRY
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Alendronate sodium
CN Fosamax
CN MK 217
CN Monosodium alendronate
MF C4 H13 N O7 P2 . Na
SR CA
LC STN Files: ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, DIOGENES, DRUGPAT, DRUGUPDATES, IMSDIRECTORY, PHAR, PROMT, RTECS*, TOXLINE, TOXLIT, USPATFULL
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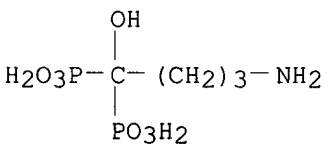

● Na

66 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
66 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:163171

REFERENCE 2: 134:105948

REFERENCE 3: 134:105846

REFERENCE 4: 133:227815

REFERENCE 5: 133:203006

REFERENCE 6: 133:155456

REFERENCE 7: 133:79271

REFERENCE 8: 133:9079

REFERENCE 9: 132:339369

REFERENCE 10: 132:260684

L138 ANSWER 40 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **124351-85-5** REGISTRY
CN Phosphonic acid, [(cycloheptylamino)methylene]bis- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Cimadronate
CN Cimadronic acid
CN Incadronic acid
CN [(Cycloheptylamino)methylene]bis(phosphonic acid)
CN [(Cycloheptylamino)methylene]diphosphonic acid
FS 3D CONCORD
MF C8 H19 N O6 P2
CI COM
SR CA
LC STN Files: ADISINSIGHT, BIOSIS, BIOTECHNO, CA, CAPLUS, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, MRCK*, PROMT, SYNTHLINE, TOXLIT, USAN, USPATFULL
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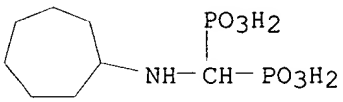
Other Sources: WHO



39 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
39 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:313639

REFERENCE 2: 133:276294

REFERENCE 3: 133:227815

REFERENCE 4: 133:203006

REFERENCE 5: 133:17634

REFERENCE 6: 133:9079

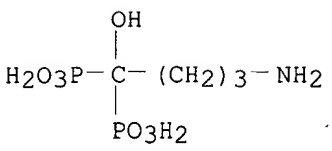
REFERENCE 7: 132:288795

REFERENCE 8: 132:288774

REFERENCE 9: 132:260710

REFERENCE 10: 132:156868

L138 ANSWER 41 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **121268-17-5** REGISTRY
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, trihydrate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Alendronate sodium hydrate
CN Sodium alendronate hydrate
MF C4 H13 N O7 P2 . 3 H2 O . Na
SR US Adopted Names Council
LC STN Files: ADISINSIGHT, CA, CAPLUS, CBNB, CIN, DRUGPAT, DRUGUPDATES, IPA, MRCK*, PHAR, RTECS*, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
CRN (66376-36-1)



● Na

● 3 H_2O

32 REFERENCES IN FILE CA (1967 TO DATE)
32 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:212746

REFERENCE 2: 134:91155

REFERENCE 3: 133:217721

REFERENCE 4: 133:9079

REFERENCE 5: 132:288773

REFERENCE 6: 132:199040

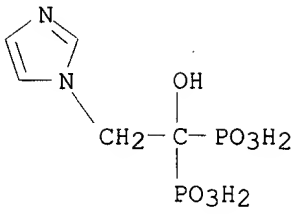
REFERENCE 7: 132:156868

REFERENCE 8: 132:69329

REFERENCE 9: 132:69328

REFERENCE 10: 132:69327

L138 ANSWER 42 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **118072-93-8** REGISTRY
CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (1-Hydroxy-2-imidazol-1-ylethylidene)diphosphonic acid
CN CGP 42446
CN Zoledronate
CN Zoledronic acid
FS 3D CONCORD
MF C5 H10 N2 O7 P2
CI COM
SR CA
LC STN Files: ADISINSIGHT, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CEN, CIN, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



71 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
72 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:173066

REFERENCE 2: 134:95352

REFERENCE 3: 134:36976

REFERENCE 4: 134:524

REFERENCE 5: 133:344627

REFERENCE 6: 133:313639

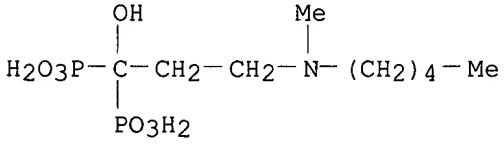
REFERENCE 7: 133:286495

REFERENCE 8: 133:252050

REFERENCE 9: 133:252041

REFERENCE 10: 133:246924

L138 ANSWER 43 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **114084-78-5** REGISTRY
CN Phosphonic acid, [1-hydroxy-3-(methylpentylamino)propylidene]bis- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Ibandronate
CN Ibandronic acid
CN [1-Hydroxy-3-(methylpentylamino)propylidene]diphosphonic acid
FS 3D CONCORD
MF C9 H23 N O7 P2
CI COM
SR CA
LC STN Files: ADISINSIGHT, ANABSTR, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CEN, CIN, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



118 REFERENCES IN FILE CA (1967 TO DATE)
10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
118 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:212746

REFERENCE 2: 134:125911

REFERENCE 3: 134:91155

REFERENCE 4: 134:36976

REFERENCE 5: 134:524

REFERENCE 6: 133:344627

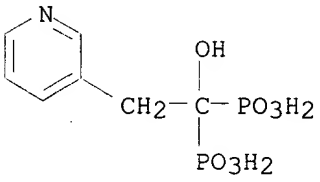
REFERENCE 7: 133:313639

REFERENCE 8: 133:290623

REFERENCE 9: 133:276294

REFERENCE 10: 133:252050

L138 ANSWER 44 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **105462-24-6** REGISTRY
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN NE 58019
CN Residronate
CN Risedronic acid
FS 3D CONCORD
MF C7 H11 N O7 P2
CI COM
SR CA
LC STN Files: ADISINSIGHT, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PROMT, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



167 REFERENCES IN FILE CA (1967 TO DATE)
12 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
167 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:212746

REFERENCE 2: 134:198075

REFERENCE 3: 134:178396

REFERENCE 4: 134:172899

REFERENCE 5: 134:163107

REFERENCE 6: 134:157507

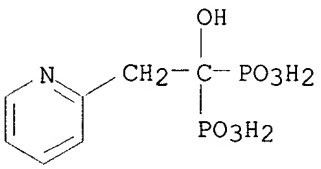
REFERENCE 7: 134:125911

REFERENCE 8: 134:125893

REFERENCE 9: 134:91155

REFERENCE 10: 134:36976

L138 ANSWER 45 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **105462-23-5** REGISTRY
CN Phosphonic acid, [1-hydroxy-2-(2-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN NE 58018
FS 3D CONCORD
MF C7 H11 N O7 P2
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



16 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
16 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:252050

REFERENCE 2: 132:59143

REFERENCE 3: 130:162737

REFERENCE 4: 130:119056

REFERENCE 5: 125:316225

REFERENCE 6: 124:45749

REFERENCE 7: 122:322504

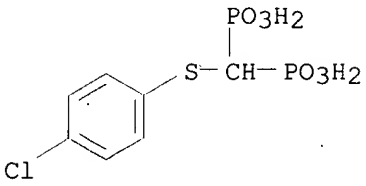
REFERENCE 8: 122:123154

REFERENCE 9: 121:245126

REFERENCE 10: 121:195927

L138 ANSWER 46 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **89987-06-4** REGISTRY
CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN SR 41319
CN Tiludronate
CN Tiludronic acid
FS 3D CONCORD
DR **96538-83-9**
MF C7 H9 Cl O6 P2 S
CI COM
LC STN Files: ADISINSIGHT, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL

(*File contains numerically searchable property data)
Other Sources: WHO



106 REFERENCES IN FILE CA (1967 TO DATE)
8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
106 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:198075

REFERENCE 2: 134:51352

REFERENCE 3: 134:36976

REFERENCE 4: 134:524

REFERENCE 5: 133:359206

REFERENCE 6: 133:344627

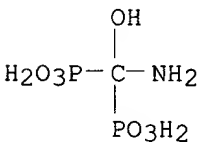
REFERENCE 7: 133:313639

REFERENCE 8: 133:252050

REFERENCE 9: 133:252041

REFERENCE 10: 133:227711

L138 ANSWER 47 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **89130-99-4** REGISTRY
CN Phosphonic acid, (aminohydroxymethylene)bis- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C H7 N O7 P2
CI COM
LC STN Files: CA, CAPLUS, TOXLIT



3 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

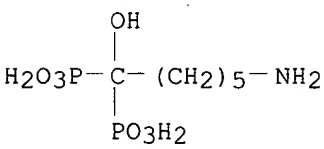
REFERENCE 1: 132:59143

REFERENCE 2: 112:207764

REFERENCE 3: 100:109162

L138 ANSWER 48 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **79778-41-9** REGISTRY
CN Phosphonic acid, (6-amino-1-hydroxyhexylidene)bis- (9CI) (CA INDEX NAME)

OTHER NAMES:
CN 6-Amino-1-hydroxyhexane-1,1-diphosphonic acid
CN 6-Amino-1-hydroxyhexylidene-1,1-bis(phosphonic acid)
CN 6-Amino-1-hydroxyhexylidenediphosphonic acid
CN Neridronate
CN Neridronic acid
FS 3D CONCORD
MF C6 H17 N O7 P2
CI COM
LC STN Files: ADISINSIGHT, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, DRUGNL, DRUGUPDATES, EMBASE, MEDLINE, PHAR, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



90 REFERENCES IN FILE CA (1967 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
90 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:172899

REFERENCE 2: 134:524

REFERENCE 3: 133:344627

REFERENCE 4: 133:313639

REFERENCE 5: 133:252050

REFERENCE 6: 133:252041

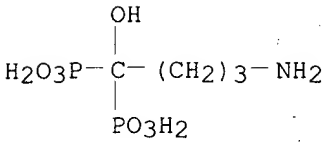
REFERENCE 7: 133:217722

REFERENCE 8: 133:217721

REFERENCE 9: 133:203006

REFERENCE 10: 133:9079

L138 ANSWER 49 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **66376-36-1** REGISTRY
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-Amino-1-hydroxybutane-1,1-diphosphonate
CN 4-Amino-1-hydroxybutane-1,1-diphosphonic acid
CN 4-Amino-1-hydroxybutane-1,1-diyldiphosphonic acid
CN 4-Amino-1-hydroxybutylidene-1,1-bis(phosphonic acid)
CN Alendronate
CN Alendronic acid
FS 3D CONCORD
MF C4 H13 N O7 P2
CI COM
LC STN Files: ADISINSIGHT, AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CIN, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PROMT, RTECS*, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



496 REFERENCES IN FILE CA (1967 TO DATE)
21 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
497 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:212746

REFERENCE 2: 134:205856

REFERENCE 3: 134:198753

REFERENCE 4: 134:198075

REFERENCE 5: 134:188046

REFERENCE 6: 134:178396

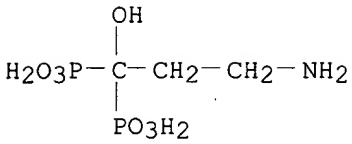
REFERENCE 7: 134:172899

REFERENCE 8: 134:163171

REFERENCE 9: 134:157508

REFERENCE 10: 134:157507

L138 ANSWER 50 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **57248-88-1** REGISTRY
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3-Amino-1-hydroxypropane-1,1-diphosphonic acid disodium salt
CN APD
CN Aredia
CN CGP 23339A
CN Disodium 3-amino-1-hydroxypropane-1,1-diphosphonate
CN Disodium pamidronate
CN Pamidronate disodium
MF C3 H11 N O7 P2 . 2 Na
CI COM
LC STN Files: ADISINSIGHT, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, DIOGENES, DRUGPAT, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, SYNTHLINE, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (40391-99-9)



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67 REFERENCES IN FILE CA (1967 TO DATE)
67 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:198075

REFERENCE 2: 134:524

REFERENCE 3: 133:203183

REFERENCE 4: 133:183064

REFERENCE 5: 133:150625

REFERENCE 6: 133:34404

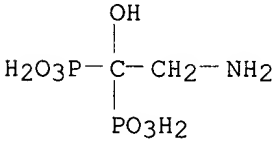
REFERENCE 7: 132:343276

REFERENCE 8: 132:260709

REFERENCE 9: 132:69329

REFERENCE 10: 132:61054

L138 ANSWER 51 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **41003-10-5** REGISTRY
CN Phosphonic acid, (2-amino-1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-Amino-1-hydroxyethane-1,1-diphosphonic acid
CN 2-Amino-1-hydroxyethylene-1,1-bisphosphonic acid
CN Ethane-1-hydroxy-2-amino-1,1-diphosphonic acid
FS 3D CONCORD
MF C2 H9 N O7 P2
CI COM
LC STN Files: CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXLIT, USPATFULL



18 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
18 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:17535

REFERENCE 2: 132:59143

REFERENCE 3: 130:322256

REFERENCE 4: 130:38467

REFERENCE 5: 128:88965

REFERENCE 6: 123:265312

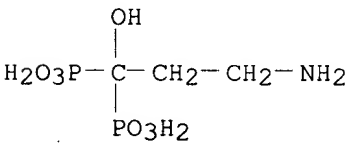
REFERENCE 7: 113:231496

REFERENCE 8: 106:5628

REFERENCE 9: 101:97713

REFERENCE 10: 101:78908

L138 ANSWER 52 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **40391-99-9** REGISTRY
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (.alpha.-Hydroxy-.gamma.-aminopropylidene)diphosphonic acid
CN (3-Amino-1-hydroxypropylidene)-1,1-bisphosponate
CN 3-Amino-1-hydroxypropane-1,1-diphosphonic acid
CN 3-Amino-1-hydroxypropylidenediphosphonic acid
CN Amidronic acid
CN Pamidronic acid
CN Propane-1-hydroxy-3-amino-1,1-diphosphonic acid
FS 3D CONCORD
MF C3 H11 N O7 P2
CI COM
LC STN Files: ADISINSIGHT, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, SPECINFO, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



465 REFERENCES IN FILE CA (1967 TO DATE)
23 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
466 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:198753

REFERENCE 2: 134:178396

REFERENCE 3: 134:173066

REFERENCE 4: 134:172899

REFERENCE 5: 134:95352

REFERENCE 6: 134:91155

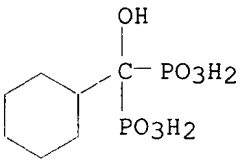
REFERENCE 7: 134:80723

REFERENCE 8: 134:36976

REFERENCE 9: 134:32972

REFERENCE 10: 134:17535

L138 ANSWER 53 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **34393-98-1** REGISTRY
CN Phosphonic acid, (cyclohexylhydroxymethylene)bis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phosphonic acid, (cyclohexylhydroxymethylene)di- (8CI)
OTHER NAMES:
CN Cyclohexylhydroxymethanediphosphonate
CN Cyclohexylhydroxymethanediphosphonic acid
CN Methanecyclohexylhydroxydiphosphonic acid
FS 3D CONCORD
MF C7 H16 O7 P2
CI COM
LC STN Files: CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXLIT, USPATFULL



9 REFERENCES IN FILE CA (1967 TO DATE)
9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 107:240873

REFERENCE 2: 95:90816

REFERENCE 3: 92:164036

REFERENCE 4: 90:61236

REFERENCE 5: 87:127290

REFERENCE 6: 86:183158

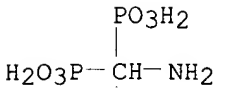
REFERENCE 7: 83:172652

REFERENCE 8: 80:74342

REFERENCE 9: 75:52779

L138 ANSWER 54 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **29712-28-5** REGISTRY
CN Phosphonic acid, (aminomethylene)bis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phosphonic acid, (aminomethylene)di- (8CI)
OTHER NAMES:
CN (Aminomethylene)di[phosphonic acid]
CN Aminomethanebis[phosphonic acid]
CN Aminomethanediphosphonic acid
CN Aminomethylenebis[phosphonic acid]
CN Aminomethylenediphosphonate
CN Methaneaminediphosphonic acid
FS 3D CONCORD
MF C H7 N O6 P2
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, IFICDB, IFIPAT, IFIUDB, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**

(**Enter CHEMLIST File for up-to-date regulatory information)



86 REFERENCES IN FILE CA (1967 TO DATE)
13 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
86 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:67398

REFERENCE 2: 133:325546

REFERENCE 3: 133:164174

REFERENCE 4: 133:146717

REFERENCE 5: 132:298659

REFERENCE 6: 132:51339

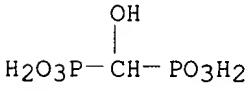
REFERENCE 7: 130:322256

REFERENCE 8: 130:38467

REFERENCE 9: 129:132964

REFERENCE 10: 128:149201

L138 ANSWER 55 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **15468-10-7** REGISTRY
CN Phosphonic acid, (hydroxymethylene)bis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phosphonic acid, (hydroxymethylene)di- (8CI)
OTHER NAMES:
CN 1-Hydroxy-1,1-diphosphonomethane
CN 1-Hydroxymethylene-1,1-bisphosphonic acid
CN HMDP
CN Hydroxymethanediphosphonic acid
CN Hydroxymethylenediphosphonate
CN Hydroxymethylenediphosphonic acid
CN MHDP
CN Oxidronic acid
FS 3D CONCORD
MF C H6 O7 P2
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK*, PHAR, PROMT, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



106 REFERENCES IN FILE CA (1967 TO DATE)
32 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
106 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:178578

REFERENCE 2: 134:178396

REFERENCE 3: 134:168857

REFERENCE 4: 134:61555

REFERENCE 5: 133:310142

REFERENCE 6: 133:309791

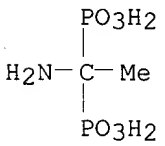
REFERENCE 7: 133:249161

REFERENCE 8: 132:83729

REFERENCE 9: 131:25531

REFERENCE 10: 130:322256

L138 ANSWER 56 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **15049-85-1** REGISTRY
CN Phosphonic acid, (1-aminoethylidene)bis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phosphonic acid, (1-aminoethylidene)di- (6CI, 7CI, 8CI)
OTHER NAMES:
CN .alpha.-Aminoethane-.alpha.,.alpha.-diphosphonic acid
CN 1-(Aminoethylidene)-1,1-diphosphonic acid
CN 1-Amino-1,1-ethanediphosphonic acid
CN 1-Amino-1,1-ethanediylbis(phosphonic acid)
CN 1-Aminoethane-1,1-phosphonic acid
CN 1-Aminoethylidene-1,1-bisphosphonic acid
CN 1-Aminoethylidenediphosphonic acid
CN AEDP
CN Ethane-1-amino-1,1-diphosphonic acid
FS 3D CONCORD
MF C2 H9 N O6 P2
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, GMELIN*, IFICDB, IFIPAT, IFIUDB, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



135 REFERENCES IN FILE CA (1967 TO DATE)
14 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
136 REFERENCES IN FILE CAPLUS (1967 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:125543

REFERENCE 2: 134:58653

REFERENCE 3: 134:38913

REFERENCE 4: 133:344627

REFERENCE 5: 132:51339

REFERENCE 6: 131:45405

REFERENCE 7: 130:349087

REFERENCE 8: 130:322256

REFERENCE 9: 130:121497

REFERENCE 10: 129:127186

L138 ANSWER 57 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **10596-23-3** REGISTRY
CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phosphonic acid, (dichloromethylene)di- (8CI)
OTHER NAMES:
CN (Dichloromethylene)bis[phosphonic acid]
CN Clodronic acid
CN Dichloromethylenediphosphonic acid
CN Methanedichlorodiphosphonic acid
FS 3D CONCORD
DR 163706-60-3
MF C H4 Cl2 O6 P2
CI COM
LC STN Files: ADISINSIGHT, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CHEMLIST, DDFU, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PHAR, RTECS*, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

545 REFERENCES IN FILE CA (1967 TO DATE)
27 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
545 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:198075

REFERENCE 2: 134:125911

REFERENCE 3: 134:112037

REFERENCE 4: 134:95438

REFERENCE 5: 134:36976

REFERENCE 6: 134:36654

REFERENCE 7: 134:16484

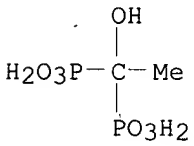
REFERENCE 8: 134:13192

REFERENCE 9: 134:13035

REFERENCE 10: 134:524

L138 ANSWER 58 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **7414-83-7** REGISTRY
CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:

CN Phosphonic acid, (1-hydroxyethylidene)di-, disodium salt (8CI)
OTHER NAMES:
CN 1-Hydroxyethane-1,1-diphosphonic acid disodium salt
CN BA 49280E
CN Didronel
CN Didronel R
CN Disodium (1-hydroxyethylidene)-1,1-bisphosphonate
CN Disodium (1-hydroxyethylidene)-1,1-diphosphonate
CN Disodium 1-hydroxy-1,1-ethanediphosphonate
CN Disodium 1-hydroxyethane-1-diphosphonate
CN Disodium 1-hydroxyethanediphosphonate
CN Disodium 1-hydroxyethylidenediphosphonate
CN Disodium ethane-1-hydroxy-1,1-diphosphonate
CN Disodium ethane-1-hydroxy-1,1-diphosphonic acid
CN Disodium ethane-1-hydroxy-1-diphosphonate
CN Disodium ethanol-1,1-diphosphonate
CN Disodium ethydronate
CN Disodium etidronate
CN Etidronate disodium
CN Fostex NZ 2
CN Ostedron
CN Sequion 10Na2
CN Sodium ethane-1-hydroxy-1,1-diphosphonate
CN Sodium ethidronate
CN Sodium ethydronate
CN Sodium etidronate
CN Turpinal 2NZ
DR 187285-10-5
MF C2 H8 O7 P2 . 2 Na
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CBNB, CHEMCATS, CHEMLIST, CIN, DIOGENES, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK*, NIOSHTIC, PHAR, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (2809-21-4)



● 2 Na

305 REFERENCES IN FILE CA (1967 TO DATE)
8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
305 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:46896

REFERENCE 2: 134:44099

REFERENCE 3: 134:21496

REFERENCE 4: 133:183064

REFERENCE 5: 133:58455

REFERENCE 6: 133:47778

REFERENCE 7: 132:293042

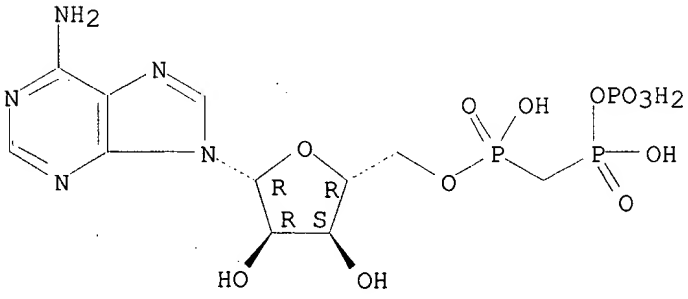
REFERENCE 8: 132:260709

REFERENCE 9: 132:83650

REFERENCE 10: 132:59008

L138 ANSWER 59 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **7292-42-4** REGISTRY
CN Adenosine, 5'-[hydrogen [[hydroxy(phosphonooxy)phosphinyl]methyl]phosphonate] (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Adenosine, 5'-(trihydrogen methylenediphosphonate), monoanhydride with phosphoric acid (8CI)
CN Adenosine, 5'-methylenediphosphonate, anhydride with H3PO4 (7CI)
OTHER NAMES:
CN (.alpha.,.beta.-Methylene)adenosine 5'-triphosphate
CN (.alpha.,.beta.-Methylene)adenosine triphosphate
CN .alpha.,.beta.-Methylene 5'-ATP
CN .alpha.,.beta.-Methylene-ATP
CN Adenosine 5'-(.alpha.,.beta.-methylenetriphosphate)
CN Adenosine 5'-(.alpha.,.beta.-methylenetriphosphonate)
CN Adenosine 5'-methylenediphosphono-P2-phosphate
CN ATP, .alpha.,.beta.-methylene-
FS STEREOSEARCH
DR 172664-67-4, 55916-39-7
MF C11 H18 N5 O12 P3
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CHEMCATS, CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, IPA, MEDLINE, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



651 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
651 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:188528

REFERENCE 2: 134:188497

REFERENCE 3: 134:188496

REFERENCE 4: 134:188494

REFERENCE 5: 134:188297

REFERENCE 6: 134:176060

REFERENCE 7: 134:173317

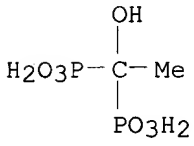
REFERENCE 8: 134:158009

REFERENCE 9: 134:110770

REFERENCE 10: 134:82686

L138 ANSWER 60 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **2809-21-4** REGISTRY
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phosphonic acid, (1-hydroxyethylidene)di- (8CI)
OTHER NAMES:
CN (1-Hydroxyethylidene)-1,1-bis(phosphonic acid)
CN (1-Hydroxyethylidene)-1,1-diphosphonic acid
CN (1-Hydroxyethylidene)bisphosphonic acid
CN (1-Hydroxyethylidene)diphosphonic acid
CN 1-Hydroxy-1,1-diphosphonoethane
CN 1-Hydroxyethane-1,1-bisphosphonic acid
CN 1-Hydroxyethane-1,1-diphosphonic acid
CN 1-Hydroxyethane-1,1-diyldiphosphonic acid
CN 1-Hydroxyethanediphosphonic acid
CN 1000SL
CN Acetodiphosphonic acid
CN Briquest ADPA 60A
CN Cublen K 60
CN Defloc EH 06
CN Dequest 16
CN Dequest 2010
CN Dequest 2010CS
CN Dequest 2015
CN Dequest Z 010
CN EHDP
CN Ethane-1-hydroxy-1,1-diphosphonic acid
CN Etidronic acid
CN Ferriox 115
CN Ferriox CY 115
CN Ferrofos 510
CN HDEPA
CN HEDP
CN Hydroxyethanediphosphonic acid
CN Ksidifon
CN Lonza 106
CN Masquol P 210
CN Mayoquest 1500
CN OEDF
CN OEDP
CN Oxyethylidenediphosphonic acid
CN RP 61
CN Sone 16
CN Tecquest 360
CN Terpil SL
CN Turpinal SL
CN Turpinal SLR
CN Wayplex
CN Xidiphone
CN Xydiphone
FS 3D CONCORD
DR 129130-42-3, 51888-66-5, 66216-98-6, 85985-26-8, 86159-18-4, 100511-44-2,

106908-76-3
MF C2 H8 O7 P2
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DETHERM*, DRUGNL, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, PHAR, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



3286 REFERENCES IN FILE CA (1967 TO DATE)
398 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3288 REFERENCES IN FILE CAPLUS (1967 TO DATE)
5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:211055

REFERENCE 2: 134:209763

REFERENCE 3: 134:209755

REFERENCE 4: 134:209747

REFERENCE 5: 134:206810

REFERENCE 6: 134:204392

REFERENCE 7: 134:198753

REFERENCE 8: 134:197890

REFERENCE 9: 134:196665

REFERENCE 10: 134:194692

L138 ANSWER 61 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **1984-15-2** REGISTRY
CN Phosphonic acid, methylenebis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phosphonic acid, methylenedi- (6CI, 7CI, 8CI)
OTHER NAMES:
CN MDP
CN Medronic acid
CN Methanebisphosphonic acid
CN Methanediphosphonic acid
CN Methylene-1,1-bisphosphonic acid
CN Methylenebis[phosphonic acid]
CN Methylenediphosphonic acid
FS 3D CONCORD
DR 63347-66-0
MF C H6 O6 P2
CI COM
LC STN Files: AGRICOLA, AIDSLINE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, TOXLINE,

TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

$H_2O_3P-CH_2-PO_3H_2$

702 REFERENCES IN FILE CA (1967 TO DATE)
353 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
705 REFERENCES IN FILE CAPLUS (1967 TO DATE)
13 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:187397

REFERENCE 2: 134:125543

REFERENCE 3: 134:117642

REFERENCE 4: 134:106509

REFERENCE 5: 134:105862

REFERENCE 6: 134:80108

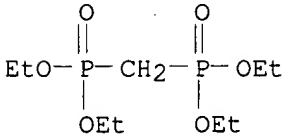
REFERENCE 7: 134:68125

REFERENCE 8: 134:61555

REFERENCE 9: 134:53165

REFERENCE 10: 134:17535

L138 ANSWER 62 OF 62 REGISTRY COPYRIGHT 2001 ACS
RN **1660-94-2** REGISTRY
CN Phosphonic acid, methylenebis-, tetraethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phosphonic acid, methylenedi-, tetraethyl ester (6CI, 7CI, 8CI)
OTHER NAMES:
CN Bis(diethylphosphono)methane
CN Methanediphosphonic acid tetraethyl ester
CN Methylenebis(diethoxyphosphine oxide)
CN Methylenebis(diethyl phosphonate)
CN Methylenebis(phosphonic acid) tetraethyl ester
CN Methylenediphosphonic acid tetraethyl ester
CN Tetraethyl methylenebisphosphonate
CN Tetraethyl methylenediphosphonate
CN Tetraethyl methylidenebisphosphonate
FS 3D CONCORD
MF C9 H22 O6 P2
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, IFICDB, IFIPAT, IFIUDB, RTECS*, SPECINFO, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



308 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
308 REFERENCES IN FILE CAPLUS (1967 TO DATE)
12 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:178602

REFERENCE 2: 134:131597

REFERENCE 3: 134:116015

REFERENCE 4: 133:281830

REFERENCE 5: 133:171382

REFERENCE 6: 133:150624

REFERENCE 7: 133:135358

REFERENCE 8: 133:120554

REFERENCE 9: 133:58868

REFERENCE 10: 132:347650

=> fil medline

FILE 'MEDLINE' ENTERED AT 11:16:57 ON 04 APR 2001

FILE LAST UPDATED: 22 MAR 2001 (20010322/UP). FILE COVERS 1958 TO DATE.

MEDLINE now contains new records from the former NLM HEALTH STAR database. These records have an Entry Date and Update Date of 20010223.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

MEDLINE has been updated with new records for the 2001 production year (20010322/UP). NLM is still in the process of preparing data. Therefore, regular updates to the file are not in place. As soon as NLM makes the regular updates available, we will process the update.

=> d his l139-

(FILE 'REGISTRY' ENTERED AT 11:02:57 ON 04 APR 2001)
SAV L138 KWON7199B/A

FILE 'REGISTRY' ENTERED AT 11:03:49 ON 04 APR 2001

FILE 'HCAPLUS' ENTERED AT 11:04:10 ON 04 APR 2001

FILE 'REGISTRY' ENTERED AT 11:05:11 ON 04 APR 2001

FILE 'MEDLINE' ENTERED AT 11:06:46 ON 04 APR 2001
L139 6159 S L6

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L140         742 S L11
L141        6887 S L139,L140
                 E DIPHOSPHONATE/CT
                 E E10+ALL
L142        6739 S E4+NT
                 E DIPHOSPHONATE#/CN
L143        3464 S E4
L144        8339 S L141-L143
                 E AUTOIMMUN/CT
L145      205946 S E17+NT
L146        3621 S E105+NT
L147         130 S L144 AND L145,L146
L148         104 S L147 AND PY<=1998
L149          25 S L148 NOT AB/FA
L150        2422 S ((DIPHOSPHONATES+NT)(L)TU.)/CT
L151           6 S L150 AND L149
L152           4 S L151 NOT PAGET/TI
L153          79 S L148 NOT L149
L154          13 S L150 AND L153
L155          66 S L153 NOT L154
L156          23 S L155 NOT TECHNETIUM TC 99M MEDRONATE/CT,CN
L157          13 S L156 NOT (99MTC OR TECHNETIUM)
L158          30 S L152,L154,L157

     FILE 'MEDLINE' ENTERED AT 11:16:57 ON 04 APR 2001

=> d all tot l158


L158 ANSWER 1 OF 30  MEDLINE
AN   1999169424     MEDLINE
DN   99169424
TI   Cyclical etidronate increases bone density in the spine and hip of
     postmenopausal women receiving long term corticosteroid treatment. A
     double blind, randomised placebo controlled study.
AU   Geusens P; Dequeker J; Vanhoof J; Stalmans R; Boonen S; Joly J; Nijs J;
     Raus J
CS   Instituut, Diepenbeek, Belgium.
SO   ANNALS OF THE RHEUMATIC DISEASES, (1998 Dec) 57 (12) 724-7.
     Journal code: 62W. ISSN: 0003-4967.
CY   ENGLAND: United Kingdom
DT   (CLINICAL TRIAL)
     Journal; Article; (JOURNAL ARTICLE)
     (RANDOMIZED CONTROLLED TRIAL)
LA   English
FS   Priority Journals
EM   199905
EW   19990502
AB   OBJECTIVE: To study the effect of cyclic etidronate in secondary
     prevention of corticosteroid induced osteoporosis. METHODS: A double
     blind, randomised placebo controlled study comparing cyclic etidronate and
     placebo during two years in 37 postmenopausal women receiving long term
     corticosteroid treatment, mainly for polymyalgia rheumatica (40% of the
     patients) and rheumatoid arthritis (30%). Bone density was measured in the
     lumbar spine, femoral neck, and femoral trochanter. RESULTS: After two
     years of treatment there was a significant difference between the groups
     in mean per cent change from baseline in bone density in the spine in
     favour of etidronate (p = 0.003). The estimated treatment difference (mean
     (SD)) was 9.3 (2.1)%. Etidronate increased bone density in the spine (4.9
     (2.1)%, p < 0.05) whereas the placebo group lost bone (-2.4 (1.6)%). At
     the femoral neck there was an estimated difference of 5.3 (2.6)% between
     the groups (etidronate: 3.6% (1.4)%, p < 0.05, placebo: -2.4 (2.1)%). The
     estimated difference at the trochanter was 8.2 (3.0) (etidronate: 9.0
     (1.5)%, p < 0.0001, placebo: 0.5 (2.3)%). No significant bone loss
     occurred in the hip in placebo treated patients. CONCLUSIONS: Cyclic
     etidronate is an effective treatment for postmenopausal women receiving
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corticosteroid treatment and is well tolerated.
CT Check Tags: Female; Human; Support, Non-U.S. Gov't
Aged
Analysis of Variance
Arthritis, Rheumatoid: DT, drug therapy
*Bone Density: DE, drug effects
*Calcium: AD, administration & dosage
Calcium: TU, therapeutic use
Double-Blind Method
Drug Administration Schedule
*Etidronate Disodium: AD, administration & dosage
Etidronate Disodium: TU, therapeutic use
Femur Neck: PP, physiopathology
*Glucocorticoids, Synthetic: AE, adverse effects
Glucocorticoids, Synthetic: TU, therapeutic use
Lumbar Vertebrae: PP, physiopathology
Middle Age
*Osteoporosis: CI, chemically induced
*Osteoporosis: PC, prevention & control
Polymyalgia Rheumatica: DT, drug therapy
Postmenopause
Statistics, Nonparametric
RN **7414-83-7 (Etidronate Disodium)**; 7440-70-2 (Calcium)
CN 0 (Glucocorticoids, Synthetic)

L158 ANSWER 2 OF 30 MEDLINE
AN 1998430703 MEDLINE
DN 98430703
TI Immune invasion of the central nervous system parenchyma and experimental allergic encephalomyelitis, but not leukocyte extravasation from blood, are prevented in macrophage-depleted mice.
AU Tran E H; Hoekstra K; van Rooijen N; Dijkstra C D; Owens T
CS Montreal Neurological Institute, Department of Microbiology and Immunology, McGill University, Quebec, Canada.
SO JOURNAL OF IMMUNOLOGY, **(1998 Oct 1)** 161 (7) 3767-75.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199812
AB Organ-specific autoimmune diseases are characterized by infiltrates, including T lymphocytes and activated macrophages. Macrophages and secondarily activated tissue resident counterparts can both present Ag to and contribute to cytokine secretion by T lymphocytes. We have previously shown a crucial role of peripheral macrophages in experimental allergic encephalomyelitis (EAE), a Th1-mediated demyelinating disease that serves as a an animal model for multiple sclerosis (MS), by their depletion using mannosylated liposome-encapsulated dichloromethylene diphosphonate (Cl2MDP). Here we describe studies to investigate the mechanisms by which macrophages contribute to the lesion formation in EAE, by studying the effect of Cl2MDP-containing mannosylated liposomes (Cl2MDP-mnL) on adoptively transferred EAE in SJL/J mice. Adoptive transfer of EAE with myelin basic protein-reactive CD4+ T cells to SJL/J mice was abrogated by Cl2MDP-mnL treatment. CD4+ T cell and MHC II+ B220+ B cell extravasation from blood vessels and Th1 cytokine production were not inhibited. However, invasion of the central nervous system intraparenchymal tissues by lymphocytes, F4/80+, Mac-1+, and MOMA-1+ macrophages was almost completely blocked after treatment with Cl2MDP-mnL. Furthermore, in Cl2MDP-mnL-treated mice, the myelin sheaths appeared completely normal, whereas, in the control groups, marked demyelination occurred. Production of TNF-alpha and inducible nitric oxide synthase, both associated with macrophage/microglial activation, was inhibited. This intervention reveals a role for macrophages in regulating the invasion of autoreactive T cells and secondary glial recruitment that ordinarily lead to demyelinating pathology in EAE and multiple sclerosis.

CT Check Tags: Animal; Female; Support, Non-U.S. Gov't
Acute Disease
*Cell Movement: IM, immunology
*Central Nervous System: IM, immunology
Central Nervous System: PA, pathology
Clodronic Acid: PD, pharmacology
CD4-Positive T-Lymphocytes: PA, pathology
Demyelinating Diseases: PA, pathology
Demyelinating Diseases: PC, prevention & control
***Encephalomyelitis, Experimental Autoimmune: IM, immunology**
Encephalomyelitis, Experimental Autoimmune: PA, pathology
Encephalomyelitis, Experimental Autoimmune: PC, prevention & control
Leukocytes, Mononuclear: DE, drug effects
Leukocytes, Mononuclear: IM, immunology
*Leukocytes, Mononuclear: PA, pathology
Liposomes: ME, metabolism
*Macrophages: IM, immunology
Macrophages: PA, pathology
Mannose: ME, metabolism
Mice
Mice, Inbred Strains
Nitric-Oxide Synthase: AI, antagonists & inhibitors
Nitric-Oxide Synthase: BI, biosynthesis
Th1 Cells: DE, drug effects
Th1 Cells: ME, metabolism
Tumor Necrosis Factor: AI, antagonists & inhibitors
Tumor Necrosis Factor: BI, biosynthesis
RN **10596-23-3 (Clodronic Acid)**; 31103-86-3 (Mannose)
CN EC 1.14.13.- (inducible nitric oxide synthase); EC 1.14.13.39 (Nitric-Oxide Synthase); 0 (Liposomes); 0 (Tumor Necrosis Factor)

L158 ANSWER 3 OF 30 MEDLINE
AN 1998377018 MEDLINE
DN 98377018
TI Abnormal bone remodelling in inflammatory arthritis.
AU Bogoch E R; Moran E
CS Orthopaedic Research Laboratory, St. Michael's Hospital, Wellesley Central Site, University of Toronto, Ont.
SO CANADIAN JOURNAL OF SURGERY, **(1998 Aug)** 41 (4) 264-71. Ref: 21
Journal code: CKJ. ISSN: 0008-428X.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199811
EW 19981102
AB Osteopenia is responsible for substantial comorbidity in patients suffering from rheumatoid arthritis and is an important factor in the surgical management of joint disease. In animal models of bone loss stimulated by inflammatory arthritis, increased bone remodelling and altered microstructure of bone have been documented. The subchondral bone plate near the joint surface is narrow and perforated by vascular inflammatory invasion, and in the shaft the thin cortices are weakened by giant resorption defects. Biomechanical tests and a mathematical model of bone strength suggest that cortical defects, much larger than those found in normal osteonal remodelling, are principally responsible for the experimentally observed loss of strength. Similarly, these defects may explain the increased femoral fracture risk in rheumatoid arthritis. The osteoclast, the cell resorbing bone, is demonstrated in increased number and activity in rheumatoid arthritis and in animal models. Bisphosphonates, drugs that inhibit osteoclast function, have been shown experimentally to reduce both focal and generalized osteopenia and to prevent loss of bone strength. Bisphosphonates also protect articular

cartilage from damage characteristic of inflammatory arthritis. The mechanism of chondroprotection may be prevention of subchondral bone resorption by the osteoclast and also an altered distribution of bone marrow cells. Thus, bisphosphonates, currently in clinical use for other bone metabolic diseases, appear to have potential as prophylaxis and treatment for osteopenia and joint damage in inflammatory arthritis.

CT Check Tags: Animal; Human
Arthritis, Rheumatoid: PA, pathology
***Arthritis, Rheumatoid: PP, physiopathology**
Bone and Bones: PA, pathology
Bone Diseases: DT, drug therapy
Bone Diseases: PP, physiopathology
*Bone Remodeling
Bone Remodeling: PH, physiology
Bone Resorption
Cartilage, Articular: DE, drug effects
Cartilage, Articular: PA, pathology
Diphosphonates: PD, pharmacology
Diphosphonates: TU, therapeutic use
Osteoblasts
Osteoclasts

CN **0 (Diphosphonates)**

L158 ANSWER 4 OF 30 MEDLINE
AN 1998279267 MEDLINE
DN 98279267
TI Differential effect of macrophage depletion on two forms of experimental uveitis evoked by pigment epithelial membrane protein (EAPU), and by melanin-protein (EMIU).
AU Broekhuyse R M; Huitinga I; Kuhlmann E D; Rooijen N V; Winkens H J
CS Institute of Ophthalmology, University of Nijmegen, The Netherlands.
SO EXPERIMENTAL EYE RESEARCH, **(1997 Dec)** 65 (6) 841-8.
Journal code: EPL. ISSN: 0014-4835.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
EW 19980802
AB The purpose of the present study was to clinically and histologically investigate the influence of macrophage depletion on the development of experimental autoimmune pigment epithelial membrane protein-induced uveitis (EAPU), and experimental melanin-protein induced uveitis (EMIU) in the Lewis rat. EAPU is mainly characterized by pigment epitheliitis. Posterior mononuclear cell accumulations enclose and destroy the retinal pigment epithelium (RPE). In EMIU the inflammation is specifically localized in the uvea. EAPU was induced by immunization with RPE membrane protein, and EMIU was evoked by immunization with purified choroidal melanin. Systemic treatment with dichloromethylene diphosphonate (Cl2MDP)-containing liposomes just before the expected beginning of the clinical signs of EAPU (at day 7 and 9 after immunization) resulted in a considerable delay of the uveitis process. In the treated animals the typical plaque shaped cell accumulations (containing many macrophages) along the RPE were lacking. Two weeks after the treatment, severe rebound EAPU developed. Local treatment by subconjunctival liposome injections did not exert any effect on EAPU. In EMIU, macrophage depletion by systemic treatment did not noticeably influence the clinical and histological development of the inflammation. Systemic treatment at the peak stage of EAPU (at day 12 and 14 after immunization) resulted in the rapid disappearance of the clinical signs of uveitis. Vitreous and anterior chamber cells were virtually absent two days later. This situation remained unchanged until the experiment was terminated two weeks later. Already deposited cell accumulations along the RPE did not regress but stopped their progression. Hematogenous macrophages thus appear to play a crucial role in the development of EAPU but the effect of early macrophage depletion on EAPU appeared to be temporary due to blood repopulation. A

possible explanation for the differential influence of macrophage depletion on EAPU and EMIU is discussed, and is based on differences in immunopathogenesis.
CT Check Tags: Animal; Comparative Study; Female; Support, Non-U.S. Gov't
***Autoimmune Diseases: IM, immunology**
Autoimmune Diseases: PA, pathology
Autoimmune Diseases: PC, prevention & control
Choroid: PA, pathology
Clodronic Acid: TU, therapeutic use
Disease Models, Animal
*Eye Proteins: IM, immunology
Immunization
Liposomes
Macrophages: DE, drug effects
Macrophages: PA, pathology
*Macrophages: PH, physiology
*Melanins: IM, immunology
Phagocytosis
*Proteins: IM, immunology
Rats
Rats, Inbred Lew
Retina: PA, pathology
*Serpins: IM, immunology
*Uveitis: IM, immunology
Uveitis: PA, pathology
Uveitis: PC, prevention & control
RN **10596-23-3 (Clodronic Acid)**
CN 0 (pigment epithelium-derived factor); 0 (Eye Proteins); 0 (Liposomes); 0 (Melanins); 0 (Proteins); 0 (Serpins)

L158 ANSWER 5 OF 30 MEDLINE
AN 1998217257 MEDLINE
DN 98217257
TI An open study of pamidronate in the treatment of refractory ankylosing spondylitis.
AU Maksymowych W P; Jhangri G S; Leclercq S; Skeith K; Yan A; Russell A S
CS Department of Medicine, University of Alberta, Edmonton, Canada.
SO JOURNAL OF RHEUMATOLOGY, **(1998 Apr)** 25 (4) 714-7.
Journal code: JWX. ISSN: 0315-162X.
CY Canada
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
EW 19980802
AB OBJECTIVE: Bisphosphonates inhibit the development of delayed type hypersensitivity chronic inflammation and suppress inflammation and cartilage/bone erosion in diverse murine arthritis models. We evaluated antiinflammatory properties of the bisphosphonate pamidronate in patients with ankylosing spondylitis (AS) refractory to nonsteroidal antiinflammatory drugs. METHODS: Patients included 14 men and 2 women. The first group of 8 patients (Group 1) received pamidronate as a 30 mg intravenous infusion once a month for 3 months, followed by a 60 mg dose once a month for an additional 3 months. Eight additional patients (Group 2) received only the 60 mg dose once a month for 3 months. Clinical assessments included the BASDAI (Bath AS Disease Activity Index), BASFI (Functional Index), and BASMI (Metrology Index), and laboratory assessments hemoglobin and erythrocyte sedimentation rate (ESR) at baseline and one month after final 60 mg dose of pamidronate. Mean BASDAI score at study entry was 6.7 for both groups. RESULTS: A significant improvement was observed in disease activity score in Group 1 after 6 monthly infusions of pamidronate (mean BASDAI 4.21; $p = 0.03$), in the BASMI score ($p = 0.01$), and the ESR ($p = 0.009$). A significant improvement in the BASMI was noted in Group 2 patients ($p = 0.007$) after 3 monthly infusions of pamidronate, but not in the BASDAI score (mean 5.01; p =

0.07) or the ESR (p = 0.12). CONCLUSION: Preliminary data suggest pamidronate may possess antiinflammatory activity in patients with AS, particularly with prolonged administration; this agent deserves further evaluation in a controlled trial.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
*Anti-Inflammatory Agents: TU, therapeutic use
Blood Sedimentation
***Diphosphonates: TU, therapeutic use**
Middle Age
***Spondylitis, Ankylosing: DT, drug therapy**
Treatment Outcome
RN **40391-99-9 (amidronate)**
CN 0 (Anti-Inflammatory Agents); **0 (Diphosphonates)**

L158 ANSWER 6 OF 30 MEDLINE
AN 1998070002 MEDLINE
DN 98070002
TI The ineffectiveness of cyclical oral clodronate on bone mineral density in glucocorticoid-treated patients with giant-cell arteritis.
AU Nordborg E; Schaufelberger C; Andersson R; Bosaeus I; Bengtsson B A
CS Division of Rheumatology, Sahlgrenska University Hospital, Goteborg, Sweden.
SO JOURNAL OF INTERNAL MEDICINE, **(1997 Nov)** 242 (5) 367-71.
Journal code: I2G. ISSN: 0954-6820.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals; Cancer Journals
EM 199803
AB OBJECTIVES AND DESIGN: The aim of the present study was to determine whether cyclic oral administration of clodronate, a bisphosphonate, every second month prevents rapid bone loss during the first year of glucocorticoid treatment in patients with giant-cell arteritis (GCA). The trial was designed as a prospective double blind study, assessing total body mineral content (BMC) and bone mineral density (BMD) using DXA technique. Supplementation of calcium was given to both groups of patients. SETTING: The outpatient clinics of the rheumatic and infectious diseases of Sahlgren University Hospital of the city of Goteborg on the west coast of Sweden. SUBJECTS: Twenty-seven patients with confirmed GCA were consecutively included during a 15-month period. RESULTS: An early influence on bone turnover was found with a temporary decrease in BMC after six months of glucocorticoid treatment, which was normalized after 12 months in both study groups. No significant differences between the patients given clodronate and calcium and the controls, who got supplementation with calcium alone, was observed at any assessment point. However, there was a significant and prolonged depression of the osteocalcin levels in the clodronate-treated patients. CONCLUSIONS: Oral administration of clodronate in a moderately high dose given cyclically every other month had no additive effect on BMD compared with calcium supplementation alone during the first year of glucocorticoid treatment. A larger material might have revealed some differences between the categories. In most patients with GCA, however, the BMD seems to recover after one year of glucocorticoid treatment, provided there is good control of the inflammation and patients are kept physically active. It needs to be elucidated whether there are subsets of patients who might benefit from bone sparing agents: women near menopause with a high turnover rate of bone, individuals who have low BMD from the start of glucocorticoid treatment or patients requiring high doses of glucocorticoids during a long period of time.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Administration, Oral
Aged

Aged, 80 and over
*Bone Density: DE, drug effects
***Clodronic Acid: PD, pharmacology**
Double-Blind Method
Drug Administration Schedule
*Glucocorticoids: TU, therapeutic use
Middle Age
Prospective Studies
***Temporal Arteritis: DT, drug therapy**
***Temporal Arteritis: PP, physiopathology**
Treatment Outcome
RN **10596-23-3 (Clodronic Acid)**
CN 0 (Glucocorticoids)

L158 ANSWER 7 OF 30 MEDLINE
AN 1998054043 MEDLINE
DN 98054043
TI Myositis ossificans complicating severe Guillain-Barre syndrome.
AU Hung J C; Appleton R E; Abernethy L
CS Department of Neurology, Royal Liverpool Children's Hospital, Alder Hey, UK.
SO DEVELOPMENTAL MEDICINE AND CHILD NEUROLOGY, **(1997 Nov)** 39 (11) 775-6.
Journal code: E83. ISSN: 0012-1622.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199802
AB We report myositis ossificans occurring in a 13-year-old boy with severe and rapidly progressive Guillain-Barre syndrome. This complication should be considered when severe musculoskeletal pain is experienced by such patients. Disodium etidronate may be of benefit in this condition.
CT Check Tags: Case Report; Human; Male
Adolescence
Cerebrospinal Fluid Proteins: AN, analysis
Etidronate Disodium: TU, therapeutic use
Immunoglobulins, Intravenous: TU, therapeutic use
Myositis Ossificans: DI, diagnosis
Myositis Ossificans: DT, drug therapy
*Myositis Ossificans: ET, etiology
Pain: ET, etiology
Polyradiculoneuropathy: CF, cerebrospinal fluid
***Polyradiculoneuropathy: CO, complications**
Polyradiculoneuropathy: TH, therapy
RN **7414-83-7 (Etidronate Disodium)**
CN 0 (Cerebrospinal Fluid Proteins); 0 (Immunoglobulins, Intravenous)

L158 ANSWER 8 OF 30 MEDLINE
AN 97402354 MEDLINE
DN 97402354
TI Matrix metalloproteinase 13 (collagenase 3) in human rheumatoid synovium.
AU Lindy O; Konttinen Y T; Sorsa T; Ding Y; Santavirta S; Ceponis A; Lopez-Otin C
CS University of Helsinki, Finland.
SO ARTHRITIS AND RHEUMATISM, **(1997 Aug)** 40 (8) 1391-9.
Journal code: 90M. ISSN: 0004-3591.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199711
EW 19971102
AB OBJECTIVE: To show the eventual presence and extent of production of matrix metalloproteinase 13 (MMP-13, or collagenase 3) in rheumatoid synovial tissue samples and extracts, and to assess the inhibition

characteristics of recombinant MMP-13. METHODS: Immunohistochemical avidin-biotin-peroxidase complex staining/morphometry was used to analyze MMP-13-positive cells in situ. Neutral salt extraction of synovial tissue, electrophoresis of the extract in different buffer systems, and Western blotting were also used. The inhibitory properties of doxycycline, clodronate, pamidronate, and D-penicillamine for recombinant enzyme were determined with a soluble type II collagen assay. RESULTS: MMP-13 was detected in fibroblast- and macrophage-like mononuclear cells in the synovial lining and stroma and in vascular endothelial cells. The overall expression of MMP-13 in these cells in the synovial stroma was high in rheumatoid arthritis (86 +/- 12%) compared with osteoarthritis (17 +/- 5%) patient samples (P = 0.0027). In a high-pH native electrophoresis gel, immunoreactivity to anti-MMP-1 and anti-MMP-13 were clearly separated, with anti-MMP-13-immunoreactive material migrating faster than anti-MMP-1-immunoreactive material. Finally, in contrast to MMP-1 and MMP-8, MMP-13 was found to be relatively resistant to the inhibitory effects of doxycycline and clodronate in vitro. CONCLUSION: Due to its localization in synovial tissue, its substrate profile, increased expression, and relative resistance to known MMP inhibitors, MMP-13 is suggested to play a major role in the pathogenesis of tissue destruction in rheumatoid arthritis.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
Aged, 80 and over
***Arthritis, Rheumatoid: EN, enzymology**
Arthritis, Rheumatoid: GE, genetics
Cartilage, Articular: CH, chemistry
Cartilage, Articular: EN, enzymology
Clodronic Acid: PD, pharmacology
Collagenases: AI, antagonists & inhibitors
*Collagenases: GE, genetics
Diphosphonates: PD, pharmacology
Immunoblotting
Immunohistochemistry
Middle Age
Osteoarthritis: EN, enzymology
Osteoarthritis: GE, genetics
Penicillamine: PD, pharmacology
Recombinant Proteins: GE, genetics
RNA, Messenger: ME, metabolism
Synovial Membrane: CH, chemistry
*Synovial Membrane: EN, enzymology

RN **10596-23-3 (Clodronic Acid); 40391-99-9 (amidronate);** 52-67-5 (Penicillamine)

CN EC 3.4.24.- (collagenase 3); EC 3.4.24.- (Collagenases); **0 (Diphosphonates)**; 0 (Recombinant Proteins); 0 (RNA, Messenger)

L158 ANSWER 9 OF 30 MEDLINE

AN 97273642 MEDLINE

DN 97273642

TI Periarticular ectopic calcinosis probably due to 1 alpha-OH-vitamin D3 therapy, and successful treatment with bisphosphonate compound in a patient with systemic lupus erythematosus.

AU Miyata M; Kurokawa M; Watanabe S; Ishikawa H; Sekine H; Ito O; Nishimaki T; Kasukawa R

CS Department of Internal Medicine II, Fukushima Medical College, Japan.

SO FUKUSHIMA JOURNAL OF MEDICAL SCIENCE, **(1996 Dec)** 42 (1-2) 39-46.
Ref: 28
Journal code: F91. ISSN: 0016-2590.

CY Japan

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW OF REPORTED CASES)

LA English

EM 199707

EW 19970703
AB We describe the case of a 25-year-old woman who developed soft tissue ectopic nephritis. Ectopic calcinosis rarely occurs in systemic lupus erythematosus (SLE) patients. This is the first detailed case report of metastatic ectopic calcinosis, one of two categories of ectopic calcinosis, probably due to 1 alpha-OH-vitamin D3 therapy. We administered disodium 3-amino-1-hydroxypropylidene-1, 1-bisphosphonate pentahydrate, a second-generation bisphosphonate, to decrease the patient's serum calcium level, and subsequently observed a dramatic decrease in severity of the ectopic calcinosis along with decreases in both the serum calcium level and the (serum calcium level)x(serum phosphate level) index. We suggest that 1 alpha-OH vitamin D3 should be used in cases of lupus nephritis with great caution.
CT Check Tags: Case Report; Female; Human
Adult
*Calcinosis: CI, chemically induced
Calcinosis: DT, drug therapy
***Diphosphonates: TU, therapeutic use**
*Finger Joint
*Hydroxycholecalciferols: AE, adverse effects
***Lupus Erythematosus, Systemic: CO, complications**
RN **40391-99-9 (amidronate)**; 41294-56-8 (1-hydroxycholecalciferol)
CN **0 (Diphosphonates)**; 0 (Hydroxycholecalciferols)

L158 ANSWER 10 OF 30 MEDLINE
AN 96316377 MEDLINE
DN 96316377
TI [Generalized osteoporosis in chronic polyarthritis--pathomechanisms and treatment approaches].
Generalisierte Osteoporose bei chronischer Polyarthritis--Pathomechanismen und Behandlungsansatze.
AU Ringe J D
CS Medizinische Klinik IV, Klinikum Leverkusen, Akademisches Lehrkrankenhaus, Universitat zu Koln.
SO ZEITSCHRIFT FUR RHEUMATOLOGIE, **(1996 May-Jun)** 55 (3) 149-57.
Ref: 49
Journal code: Y0V. ISSN: 0340-1855.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA German
FS Priority Journals
EM 199612
AB Juxtaarticular osteoporosis is a typical x-ray symptom of rheumatoid arthritis and is an early radiological criterion of the disease before destructive changes of joints can be seen. A systemic osteoporosis, independent from corticoid treatment, will develop significantly later. Nevertheless both conditions have some pathogenetic mechanisms in common. The risk of generalized osteoporosis in rheumatoid arthritis correlates with the degree of inflammatory activity. Different cytokines originating from the affected joints can be measured in plasma at increased levels and augment osteoclastic activity in bone tissue. During the early phase of disease the best prevention of osteoporosis is therefore adequate suppression of inflammation. Taking into account these mechanisms, corticoid treatment may be osteoprotective. Clinical manifestation of systemic osteoporosis in rheumatic patients depends on bone mass at onset of disease, on the activity of inflammation, and on additional negative effects on bone mass due to corticoids and immobility.
CT Check Tags: Human
Adrenal Cortex Hormones: AD, administration & dosage
Adrenal Cortex Hormones: AE, adverse effects
***Arthritis, Rheumatoid: CO, complications**
Arthritis, Rheumatoid: DI, diagnosis
Arthritis, Rheumatoid: DT, drug therapy
Bone Density: DE, drug effects

Bone Density: PH, physiology
Calcitonin: AD, administration & dosage
Calcium, Dietary: AD, administration & dosage
Combined Modality Therapy
Cytokines: BL, blood
Diphosphonates: AD, administration & dosage
English Abstract
Osteoclasts: DE, drug effects
Osteoclasts: PH, physiology
Osteoporosis: DI, diagnosis
Osteoporosis: DT, drug therapy
*Osteoporosis: ET, etiology
Risk Factors
Vitamin D: AD, administration & dosage
RN 1406-16-2 (Vitamin D); 9007-12-9 (Calcitonin)
CN 0 (Adrenal Cortex Hormones); 0 (Calcium, Dietary); 0 (Cytokines); **0 (Diphosphonates)**

L158 ANSWER 11 OF 30 MEDLINE
AN 96193600 MEDLINE
DN 96193600
TI Increased bone mass with pamidronate treatment in rheumatoid arthritis. Results of a three-year randomized, double-blind trial.
AU Eggelmeijer F; Papapoulos S E; van Paassen H C; Dijkmans B A; Valkema R; Westedt M L; Landman J O; Pauwels E K; Breedveld F C
CS University Hospital, Leiden, The Netherlands.
SO ARTHRITIS AND RHEUMATISM, **(1996 Mar)** 39 (3) 396-402.
Journal code: 90M. ISSN: 0004-3591.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199607
AB OBJECTIVES: Osteoporosis is a frequent complication of rheumatoid arthritis (RA). We therefore investigated the effect of oral pamidronate therapy as a specific bone-sparing agent in RA. METHODS: The study design was a 3-year randomized, double-blind trial of 300 mg oral pamidronate/day compared with placebo in 105 RA patients. Bone mineral density (BMD) measured at 12-month intervals was the primary efficacy parameter. RESULTS: In 3 years, lumbar spine and forearm BMD increased significantly in the pamidronate-treated group (by 8.4 +/- 6.9% [mean =/- SEMI] [P < 0.00011 and 5.2 =/- 6.5% [P < 0.005], respectively), compared with nonsignificant changes in the placebo-treated patients (increase of 0.6 =/- 5.2% and decrease of 1.2 =/- 5.8%, respectively). Femoral neck BMD increased in the pamidronate-treated group (by 2.6 =/- 8.6%) and decreased significantly in the placebo-treated group (by 4.0=/- 1.3% [P < 0.005]). The changes in BMD with time at all 3 measurement sites were significantly different between the treatment groups (P < 0.0001). Changes in radiographic signs of joint damage and in disease activity were similar in the 2 groups. CONCLUSION: The present study provides the first evidence that long-term treatment with an orally administered bisphosphonate overcomes bone loss and increases bone mass when compared with placebo. This finding may have significance with regard to the treatment of patients with RA.
CT Check Tags: Female; Human; Male
Adult
Aged
Anti-Inflammatory Agents, Non-Steroidal: AD, administration & dosage
***Arthritis, Rheumatoid: DT, drug therapy**
Arthritis, Rheumatoid: PA, pathology
Bone and Bones: DE, drug effects
Bone and Bones: ME, metabolism
*Bone and Bones: PA, pathology
Bone Density: DE, drug effects

***Diphosphonates: AD, administration & dosage**
Diphosphonates: TO, toxicity
Double-Blind Method
Injections, Intravenous
Middle Age
Placebos
Walking
RN **40391-99-9 (amidronate)**
CN 0 (Anti-Inflammatory Agents, Non-Steroidal); **0 (Diphosphonates);**
0 (Placebos)

L158 ANSWER 12 OF 30 MEDLINE
AN 96111183 MEDLINE
DN 96111183
TI Treatment of osteoporosis of rheumatoid arthritis [letter].
AU Cantatore F P; Carrozzo M
SO CLINICAL RHEUMATOLOGY, **(1995 Sep)** 14 (5) 594-5.
Journal code: DI6. ISSN: 0770-3198.
CY Belgium
DT Letter
LA English
FS Priority Journals
EM 199604
CT Check Tags: Human
***Arthritis, Rheumatoid: CO, complications**
Diphosphonates: TU, therapeutic use
*Osteoporosis: DT, drug therapy
*Osteoporosis: ET, etiology
Osteoporosis: PP, physiopathology
CN **0 (Diphosphonates)**

L158 ANSWER 13 OF 30 MEDLINE
AN 95404532 MEDLINE
DN 95404532
TI Low dose corticosteroid associated osteoporosis in rheumatoid arthritis and its prophylaxis and treatment: bones of contention [editorial].
AU Dequeker J; Westhovens R
SO JOURNAL OF RHEUMATOLOGY, **(1995 Jun)** 22 (6) 1013-9. Ref: 66
Journal code: JWX. ISSN: 0315-162X.
CY Canada
DT Editorial
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199512
CT Check Tags: Female; Human
*Adrenal Cortex Hormones: AE, adverse effects
Adrenal Cortex Hormones: TU, therapeutic use
***Arthritis, Rheumatoid: DT, drug therapy**
Bone Density: DE, drug effects
Diphosphonates: TU, therapeutic use
Dose-Response Relationship, Drug
Estrogen Replacement Therapy
Fluorides: TU, therapeutic use
*Osteoporosis: CI, chemically induced
*Osteoporosis: PC, prevention & control
Osteoporosis: TH, therapy
Vitamin D: ME, metabolism
RN 1406-16-2 (Vitamin D)
CN 0 (Adrenal Cortex Hormones); **0 (Diphosphonates);** 0 (Fluorides)

L158 ANSWER 14 OF 30 MEDLINE
AN 95362762 MEDLINE
DN 95362762
TI Glucocorticoid-induced osteoporosis.

AU Hahn B H; Mazzaferri E L
CS University of California School of Medicine, Los Angeles, USA..
SO HOSPITAL PRACTICE (OFFICE EDITION), **(1995 Aug 15)** 30 (8) 45-9, 52-3; discussion 53-6.
Journal code: HPO. ISSN: 8750-2836.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199511
AB High-dose treatment of more than three months' duration reduces bone mass, regardless of the patient's age, sex, or race. Because bone loss is most severe during the first six to 12 months of treatment, prophylaxis to preserve bone--with calcium, vitamin D, a bisphosphonate, and exercise--should begin as soon as the clinical situation permits rather than after the disease has been brought under control.
CT Check Tags: Case Report; Female; Human
Adolescence
Aged
Calcium: TU, therapeutic use
Combined Modality Therapy
Diphosphonates: TU, therapeutic use
Drug Therapy, Combination
Exercise Therapy
Glucocorticoids, Synthetic: AD, administration & dosage
*Glucocorticoids, Synthetic: AE, adverse effects
Iatrogenic Disease: PC, prevention & control
Lupus Erythematosus, Systemic: CO, complications
Lupus Erythematosus, Systemic: DT, drug therapy
*Osteoporosis: CI, chemically induced
Osteoporosis: PC, prevention & control
Polymyalgia Rheumatica: CO, complications
Polymyalgia Rheumatica: DT, drug therapy
Prednisone: AD, administration & dosage
Prednisone: AE, adverse effects
Time Factors
Vitamin D: TU, therapeutic use
RN 1406-16-2 (Vitamin D); 53-03-2 (Prednisone); 7440-70-2 (Calcium)
CN **0 (Diphosphonates)**; 0 (Glucocorticoids, Synthetic)

L158 ANSWER 15 OF 30 MEDLINE
AN 95262295 MEDLINE
DN 95262295
TI Macrophages in T cell line-mediated, demyelinating, and chronic relapsing experimental autoimmune encephalomyelitis in Lewis rats.
AU Huitinga I; Ruuls S R; Jung S; Van Rooijen N; Hartung H P; Dijkstra C D
CS Department of Cell Biology and Immunology, Faculty of Medicine, Vrije Universiteit, Amsterdam, The Netherlands.
SO CLINICAL AND EXPERIMENTAL IMMUNOLOGY, **(1995 May)** 100 (2) 344-51.
Journal code: DD7. ISSN: 0009-9104.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199508
AB About 50% of the mononuclear cells in the perivascular lesions in the central nervous system (CNS) of rats suffering from experimental allergic encephalomyelitis (EAE) are blood-borne macrophages. In this study we investigated the role of these macrophages in different variants of EAE, using a liposome-mediated macrophage depletion technique. Intravenously injected liposomes containing dichloromethylene diphosphonate (Cl2MDP) are ingested by macrophages and cause temporary and selective elimination of these cells. Macrophage depletion during EAE induced by a T cell line specific for myelin basic protein (MBP; T cell-EAE) suppresses development of neurological signs of EAE. T cell-EAE with pronounced demyelination as induced by an additionally injected MoAb directed against myelin

oligodendrocyte glycoprotein (MOG) was also significantly ameliorated after macrophage depletion. During chronic relapsing EAE (CR-EAE) the occurrence of relapses was prevented or suppressed, provided that the liposomes were injected before the initiation of a putative relapse. A chronic progressive course of CR-EAE was not modified by Cl2MDP containing liposome treatment. Histologic examination of the CNS of liposome-treated animals confirmed decreased infiltration of macrophages into the parenchyma in the rats with T cell and AD-EAE, whereas T cells were still present.

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
Clodronic Acid: PD, pharmacology
Cyclosporine: PD, pharmacology
Demyelinating Diseases: IM, immunology
***Encephalomyelitis, Experimental Autoimmune: IM, immunology**
Encephalomyelitis, Experimental Autoimmune: PA, pathology
*Macrophages: IM, immunology
Rats
Rats, Inbred Lew
T-Lymphocytes: IM, immunology

RN **10596-23-3 (Clodronic Acid)**; 59865-13-3 (Cyclosporine)

L158 ANSWER 16 OF 30 MEDLINE
AN 95173891 MEDLINE
DN 95173891
TI Clinical and biochemical response to single infusion of pamidronate in patients with active rheumatoid arthritis: a double blind placebo controlled study.
AU Eggelmeijer F; Papapoulos S E; van Paassen H C; Dijkmans B A; Breedveld F C
CS Department of Rheumatology, Leiden, The Netherlands..
SO JOURNAL OF RHEUMATOLOGY, **(1994 Nov)** 21 (11) 2016-20.
Journal code: JWX. ISSN: 0315-162X.
CY Canada
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199506
AB OBJECTIVE. To assess the effects of 3-amino-1-hydroxypropylidine-1,1-bisphosphonate (pamidronate) in rheumatoid arthritis (RA). METHODS. Thirty patients with active RA were randomly allocated to receive a single intravenous infusion of placebo, 20 mg pamidronate, or 40 mg pamidronate. RESULTS. Pamidronate treatment resulted in a rapid and sustained reduction in urinary calcium and hydroxyproline excretions. A sustained reduction in serum corrected calcium was only noted in the group treated with 40 mg pamidronate. In both groups treated with pamidronate a temporary increase in serum parathyroid hormone was noted. Compared to the placebo group clinical variables of disease activity improved significantly in both groups treated with aminohydroxypropylidine bisphosphonate. The erythrocyte sedimentation rate and serum C-reactive protein levels improved significantly in patients treated with 40 mg pamidronate. No serious side effects were documented. CONCLUSION. A single infusion of pamidronate in patients with RA is safe, suppresses bone resorption, and reduces disease activity. It is suggested that the effect on disease activity is dose dependent.
CT Check Tags: Comparative Study; Female; Human; Male
Adult
Arthritis, Rheumatoid: BL, blood
***Arthritis, Rheumatoid: DT, drug therapy**
Arthritis, Rheumatoid: ME, metabolism
Arthritis, Rheumatoid: UR, urine
Bone and Bones: DE, drug effects
*Bone and Bones: ME, metabolism
Bone Resorption: DT, drug therapy
Calcium: BL, blood

Calcium: UR, urine
Diphosphonates: AE, adverse effects
***Diphosphonates: TU, therapeutic use**
Double-Blind Method
Hydroxyproline: UR, urine
Infusions, Intravenous
Middle Age
Radioimmunoassay
RN **40391-99-9 (amidronate)**; 51-35-4 (Hydroxyproline); 7440-70-2 (Calcium)
CN **0 (Diphosphonates)**

L158 ANSWER 17 OF 30 MEDLINE
AN 95138952 MEDLINE
DN 95138952
TI Intermittent cyclic therapy with etidronate in the prevention of corticosteroid induced bone loss.
AU Adachi J; Cranney A; Goldsmith C H; Bensen W G; Bianchi F; Cividino A; Craig G L; Kaminska E; Sebaldt R J; Papaioannou A; et al
CS St. Joseph's Hospital, McMaster University, Hamilton, ON, Canada..
SO JOURNAL OF RHEUMATOLOGY, **(1994 Oct)** 21 (10) 1922-6.
Journal code: JWX. ISSN: 0315-162X.
CY Canada
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199505
AB OBJECTIVE. To assess the potential efficacy of intermittent cyclic therapy (ICT) with etidronate in the treatment of patients with corticosteroid induced osteoporosis. METHODS. Cohort study in a tertiary care university affiliated hospital in corticosteroid treated patients, with polymyalgia rheumatica, asthma, systemic lupus erythematosus, rheumatoid arthritis, or temporal arteritis, examining the effects of ICT etidronate. Patients were included if they were taking corticosteroids for a minimum of one year. Comparison patients were those who had been taking corticosteroids for a minimum of one year and who had not been treated with etidronate or other medication which might alter bone metabolism. A total of 68 patients were included from 253 considered. The mean (SD) dose of prednisone in the ICT etidronate treated patients was 9.3 (6.2) mg and in the comparison patients 9.4 (5.9) mg. The duration of prednisone therapy was 7.8 (5.8) years and 3.4 (4.2) years, respectively ($p2 < 0.001$). An analysis of covariance demonstrated that this difference did not alter our primary outcome measure. The primary outcome measure was the difference in the percentage change from baseline to one year of followup in bone mineral density (BMD) of the lumbar spine between treatment and comparison groups. RESULTS. ICT etidronate resulted in a statistically significant and clinically important increase in BMD. The BMD of the lumbar spine increased by 3.82% (0.65%), [95% confidence interval (CI), 2.51 to 5.14%] in the 35 ICT etidronate treated patients and decreased by 1.78% (0.76%), [95% CI, -3.34 to -0.23%] in the 33 comparison patients after 12 months ($p2 < 0.0001$). CONCLUSIONS. ICT etidronate prevented loss of vertebral bone density in patients with corticosteroid induced osteoporosis. Controlled, double blind, prospective trials with longer followup are needed to confirm these results and to demonstrate that increases in bone mass translate into decreased fracture rates.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
*Adrenal Cortex Hormones: AE, adverse effects
Adrenal Cortex Hormones: TU, therapeutic use
Adult
Aged
Arthritis, Rheumatoid: DT, drug therapy
Bone Density
Cohort Studies
Dose-Response Relationship, Drug

Double-Blind Method
Etidronate Disodium: AD, administration & dosage
*Etidronate Disodium: TU, therapeutic use
Femur Neck: PH, physiology
Follow-Up Studies
Lumbar Vertebrae: PH, physiology
Lupus Erythematosus, Systemic: DT, drug therapy
Middle Age
*Osteoarthritis: CI, chemically induced
*Osteoarthritis: PC, prevention & control
Pilot Projects
RN **7414-83-7 (Etidronate Disodium)**
CN 0 (Adrenal Cortex Hormones)

L158 ANSWER 18 OF 30 MEDLINE
AN 94377906 MEDLINE
DN 94377906
TI Double blind radiological assessment of continuous oral pamidronic acid in patients with rheumatoid arthritis.
AU Maccagno A; Di Giorgio E; Roldan E J; Caballero L E; Perez Lloret A
CS Department of Rheumatology, French Hospital, Buenos Aires, Argentina.
SO SCANDINAVIAN JOURNAL OF RHEUMATOLOGY, **(1994)** 23 (4) 211-4.
Journal code: UD1. ISSN: 0300-9742.
CY Norway
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199412
AB Continuous oral pamidronate (APD), 1000 mg/day, was administered to 14 patients with rheumatoid arthritis. A control group of 13 patients with similar conditions received placebo under a double blind randomized study design. Periarticular erosion scores were significantly higher in the control group after 12 months treatment. This was attributed to a deterioration in this group rather than to an improvement in the APD treated one. By contrast, intraarticular narrowing score was not influenced by APD. Tolerance to oral APD was acceptable in all patients.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Administration, Oral
Adult
Arthritis, Rheumatoid: DT, drug therapy
***Arthritis, Rheumatoid: RA, radiography**
Cartilage, Articular: RA, radiography
***Diphosphonates: AD, administration & dosage**
Double-Blind Method
Drug Administration Schedule
Foot: RA, radiography
Hand: RA, radiography
Middle Age
Severity of Illness Index
RN **40391-99-9 (amidronate)**
CN **0 (Diphosphonates)**

L158 ANSWER 19 OF 30 MEDLINE
AN 94207702 MEDLINE
DN 94207702
TI Intermittent cyclical etidronate in the prevention of corticosteroid-induced bone loss.
AU Mulder H; Struys A
CS Gezondheidscentrum Zuidplein, Rotterdam, The Netherlands.
SO BRITISH JOURNAL OF RHEUMATOLOGY, **(1994 Apr)** 33 (4) 348-50.
Journal code: B1T. ISSN: 0263-7103.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199407
AB We conducted a prospective study of etidronate's effects on corticosteroid-induced bone loss in postmenopausal women with temporal arteritis for whom high-dose prednisone therapy was indicated. Group A (n = 10) received etidronate (400 mg/day for 2 weeks, then 11 weeks off etidronate; four cycles total) and prednisone: Group B (n = 10) received only prednisone. Vertebral bone mineral density (BMD) was measured blinded by dual X-ray absorptiometry. At 3, 6 and 12 months, vertebral BMD was significantly ($P < 0.01$) increased in Group A and decreased in Group B, based on mean actual and percent changes in BMD and mean changes in BMD Z-score from baseline. Between-group comparisons were also significant ($P < 0.002$) at each time point. No adverse events related to etidronate treatment were reported. Our results suggest that corticosteroid-induced bone loss may be prevented by instituting intermittent cyclical etidronate therapy when high-dose prednisone therapy is begun. Further research into bisphosphonate use in corticosteroid-induced bone loss (with larger patient populations, longer follow-up and fracture assessment) is warranted.
CT Check Tags: Female; Human
*Adrenal Cortex Hormones: AE, adverse effects
Aged
Aged, 80 and over
Bone Density: DE, drug effects
Drug Administration Schedule
*Etidronate Disodium: AE, adverse effects
Etidronate Disodium: TU, therapeutic use
Middle Age
*Osteoporosis, Postmenopausal: CI, chemically induced
Osteoporosis, Postmenopausal: ME, metabolism
Prednisone: AD, administration & dosage
Prednisone: AE, adverse effects
Prednisone: TU, therapeutic use
Temporal Arteritis: DT, drug therapy
RN 53-03-2 (Prednisone); **7414-83-7 (Etidronate Disodium)**
CN 0 (Adrenal Cortex Hormones)

L158 ANSWER 20 OF 30 MEDLINE
AN 94103837 MEDLINE
DN 94103837
TI Selective elimination of macrophages by dichlormethylene diphosphonate-containing liposomes suppresses experimental autoimmune neuritis.
AU Jung S; Huitinga I; Schmidt B; Zielasek J; Dijkstra C D; Toyka K V; Hartung H P
CS Department of Neurology, Julius-Maximilians-Universitat, Wurzburg, Germany..
SO JOURNAL OF THE NEUROLOGICAL SCIENCES, **(1993 Nov)** 119 (2) 195-202.
Journal code: JBJ. ISSN: 0022-510X.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199404
AB The injection of liposome-encapsulated dichlormethylene diphosphonate (Cl2MDP) constitutes an effective method to selectively eliminate phagocytic cells from spleen, liver and the circulation. We evaluated the effect of Cl2MDP-liposomes on the course of actively induced and adoptively transferred experimental autoimmune neuritis (EAN), both animal models of the human Guillain-Barre syndrome. Injection of Cl2MDP-liposomes 11 and 13 days postimmunization (p.i.) of Lewis rats with bovine peripheral nerve myelin efficiently prevented clinical signs of EAN up to day 15 p.i., when all control animals were affected. Thereafter, EAN

gradually also developed in Cl2MDP-liposome-treated rats, but until day 19 disease was significantly milder than in control rats injected with buffer-filled liposomes. Adoptive transfer EAN (AT-EAN) induced by injection of activated P2-specific T cells could be suppressed even more markedly by application of Cl2MDP-liposomes 1, 3, and 6 days after cell transfer. Efficient suppression of AT-EAN by Cl2MDP-liposomes rules out the possibility that EAN is prevented due to interference with the induction phase of this experimental disease and confirms that macrophages are important effector cells during EAN. Selective suppression of phagocytic cell function by drug-containing liposomes may hold promise as a novel treatment of demyelinating autoimmune diseases of the nervous system.

CT Check Tags: Animal; Female; Support, Non-U.S. Gov't
Behavior, Animal: PH, physiology
***Clodronic Acid: PD, pharmacology**
Electrophysiology
Liposomes
*Macrophages: DE, drug effects
Myelin Sheath: IM, immunology
***Neuritis, Experimental Allergic: IM, immunology**
Neuritis, Experimental Allergic: PA, pathology
Neuritis, Experimental Allergic: PX, psychology
Rats
Rats, Inbred Lew
Sciatic Nerve: PA, pathology
Spinal Nerve Roots: PA, pathology

RN **10596-23-3 (Clodronic Acid)**
CN 0 (Liposomes)

L158 ANSWER 21 OF 30 MEDLINE
AN 91284442 MEDLINE
DN 91284442
TI Treatment and prevention of osteoporosis in juvenile chronic arthritis with disodium clodronate.
AU Lepore L; Pennesi M; Barbi E; Pozzi R
CS Pediatric Department, University of Trieste, Istituto per l'Infanzia Burlo Garofolo, Italy.
SO CLINICAL AND EXPERIMENTAL RHEUMATOLOGY, **(1991 Jan-Feb)** 9 Suppl 6 33-5.
Journal code: DFA. ISSN: 0392-856X.
CY Italy
DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199110
AB Osteoporosis is one of the most difficult problems in the management of Chronic Juvenile Arthritis (JCA). The available data suggest that bone loss results from multifactorial processes which lead to bone degradation through the activation of osteoclasts. Biphosphonates are synthetic factors that, once localized on the surface of hydroxyapatite crystals, do not allow either the production or destruction of the crystals. This activity seems to be due to cytotoxicity against osteoclasts and to inhibition of prostaglandin E2 synthesis. There is some evidence that these drugs are effective in the treatment of osteoporosis in several diseases. In an attempt to reduce or prevent osteoporosis in children affected by JCA we started a trial with disodium clodronate, a type of biphosphonate. Thirteen patients were enrolled in the study: 7 received disodium clodronate and 6 acted as control subjects. Before starting the therapy and after one year we performed a CT scan to evaluate the mineral bone density in all patients. The mean bone density increased from a bone mineral content of 129 mg/cc before treatment to 134 mg/cc after treatment (8% increase); control patients passed from 123 mg/cc to 115 mg/cc (7% decrease) in the same period. Only one child stopped treatment because of gastrointestinal side effects. The small number of patients enrolled in

the trial does not allow any definite conclusions to be drawn, but the data are interesting and worthy of further study.
CT Check Tags: Human
Arthritis, Juvenile Rheumatoid: CO, complications
***Arthritis, Juvenile Rheumatoid: DT, drug therapy**
Arthritis, Juvenile Rheumatoid: ME, metabolism
Bone Density: DE, drug effects
Calcium: BL, blood
Calcium: UR, urine
Child
Child, Preschool
Diphosphonates: AE, adverse effects
***Diphosphonates: TU, therapeutic use**
Osteoporosis: ET, etiology
*Osteoporosis: PC, prevention & control
RN 7440-70-2 (Calcium)
CN **0 (Diphosphonates)**

L158 ANSWER 22 OF 30 MEDLINE
AN 91279593 MEDLINE
DN 91279593
TI Endocrinology.
AU Baxter M A; Sheppard M C
CS Department of Medicine, University of Birmingham, Queen Elizabeth Hospital, Edgbaston, UK..
SO POSTGRADUATE MEDICAL JOURNAL, **(1991 Jan)** 67 (783) 23-32. Ref: 47
Journal code: PFX. ISSN: 0032-5473.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199110
CT Check Tags: Human
Adult
Diphosphonates: TU, therapeutic use
*Endocrine Diseases: TH, therapy
Graves' Disease: DT, drug therapy
Hypercalcemia: ET, etiology
Neoplasms: CO, complications
Osteoporosis: CI, chemically induced
Ovulation Induction
Proteins: PH, physiology
Somatotropin: PH, physiology
Somatotropin: TU, therapeutic use
Thyroid Hormones: PH, physiology
Thyroxine: AE, adverse effects
Turner's Syndrome: DT, drug therapy
RN 7488-70-2 (Thyroxine); 9002-72-6 (Somatotropin)
CN 0 (parathyroid hormone-related protein); **0 (Diphosphonates)**; 0 (Thyroid Hormones)

L158 ANSWER 23 OF 30 MEDLINE
AN 91191305 MEDLINE
DN 91191305
TI Osteoporosis in rheumatoid arthritis--the clinical viewpoint [editorial].
AU Woolf A D
SO BRITISH JOURNAL OF RHEUMATOLOGY, **(1991 Apr)** 30 (2) 82-4.
Journal code: B1T. ISSN: 0263-7103.
CY ENGLAND: United Kingdom
DT Editorial
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199107

CT Check Tags: Human
Anti-Inflammatory Agents: TU, therapeutic use
***Arthritis, Rheumatoid: CO, complications**
Arthritis, Rheumatoid: PA, pathology
Arthritis, Rheumatoid: PP, physiopathology
Biological Markers
Bone and Bones: PA, pathology
Bone Diseases, Metabolic: CO, complications
Diphosphonates: TU, therapeutic use
Estrogens: TU, therapeutic use
Osteogenesis
*Osteoporosis: CO, complications
Osteoporosis: DT, drug therapy
CN 0 (Biological Markers); **0 (Diphosphonates)**; 0 (Estrogens)

L158 ANSWER 24 OF 30 MEDLINE
AN 91011242 MEDLINE
DN 91011242
TI Suppression of experimental allergic encephalomyelitis in Lewis rats after elimination of macrophages.
AU Huitinga I; van Rooijen N; de Groot C J; Uitdehaag B M; Dijkstra C D
CS Department of Cell Biology, Medical Faculty, Vrije Universiteit, Amsterdam, The Netherlands.
SO JOURNAL OF EXPERIMENTAL MEDICINE, **(1990 Oct 1)** 172 (4) 1025-33.
Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199101
AB Almost 50% of the cells infiltrating the central nervous system (CNS) of animals with experimental allergic encephalomyelitis (EAE) are macrophages (M psi). To investigate the role of the M psi in the pathogenesis of EAE, we eliminated M psi by means of mannosylated liposomes containing dichloromethylene diphosphonate (Cl2MDP). Cl2MDP-containing liposomes injected intravenously eliminate M psi in spleen and liver. Incorporation of mannose into the lipid layers enables the liposomes to pass the blood-brain barrier (BBB). Injections of Cl2MDP-containing mannose liposomes intravenously shortly before the appearance of clinical signs, markedly suppressed the expression of clinical signs of EAE. This suppression was accompanied by a marked reduction of infiltrated M psi in the CNS. Cl2MDP-containing liposomes without mannose incorporated had no effect. Cl2MDP-containing mannosylated liposomes had no effect on plasma corticosterone levels compared with injections of saline; thus, the suppression of expression of EAE was not corticosterone mediated. These results show that the M psi within the CNS play an important role in the pathogenesis of EAE.
CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
Antigens, CD4: PH, physiology
Brain: PA, pathology
Clodronic Acid: AD, administration & dosage
Clodronic Acid: PD, pharmacology
Corticosterone: BL, blood
***Encephalomyelitis, Experimental Autoimmune: ET, etiology**
Encephalomyelitis, Experimental Autoimmune: PA, pathology
Encephalomyelitis, Experimental Autoimmune: PC, prevention & control
Liposomes
*Macrophages: PH, physiology
Rats
Rats, Inbred Lew
T-Lymphocytes: PH, physiology
RN **10596-23-3 (Clodronic Acid)**; 50-22-6 (Corticosterone)
CN 0 (Antigens, CD4); 0 (Liposomes)

L158 ANSWER 25 OF 30 MEDLINE

AN 89303431 MEDLINE
DN 89303431
TI Effects of aminobisphosphonate infusion on biochemical indices of bone metabolism in rheumatoid arthritis.
AU Tan P L; Ames R; Yeoman S; Ibbertson H K; Caughey D E
CS Department of Immunobiology, University of Auckland School of Medicine, New Zealand..
SO BRITISH JOURNAL OF RHEUMATOLOGY, **(1989 Aug)** 28 (4) 325-8.
Journal code: B1T. ISSN: 0263-7103.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198910
AB In a phase 1 study, seven patients with classical rheumatoid arthritis were treated with intravenous 3-amino-1-hydroxypropylidene-1-1-bisphosphonate (APD). Following this treatment, bone resorption as measured by fasting urine calcium/creatinine and hydroxyproline/creatinine ratios, was reduced. This was sustained for 6 months in only three patients. Elevations of these ratios often coincided with flares of active arthritis in the remaining four patients. Bone turnover as measured by serum osteocalcin levels was reduced in all patients but serum alkaline phosphatase levels remained unchanged. There was no consistent improvement in clinical indices of disease activity.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
Arthritis, Rheumatoid: DT, drug therapy
***Arthritis, Rheumatoid: UR, urine**
Bone and Bones
Calcium: UR, urine
Calcium-Binding Proteins: BL, blood
Creatinine: UR, urine
Diphosphonates: AD, administration & dosage
***Diphosphonates: TU, therapeutic use**
Drug Evaluation
Hydroxyproline: UR, urine
Infusions, Intravenous
Middle Age
RN 104982-03-8 (Osteocalcin); **40391-99-9 (amidronate)**; 51-35-4 (Hydroxyproline); 60-27-5 (Creatinine); 7440-70-2 (Calcium)
CN 0 (Calcium-Binding Proteins); **0 (Diphosphonates)**

L158 ANSWER 26 OF 30 MEDLINE
AN 89272261 MEDLINE
DN 89272261
TI Clinical, biochemical, and radiographic effects of aminohydroxypropylidene bisphosphonate treatment in rheumatoid arthritis.
AU Ralston S H; Hacking L; Willocks L; Bruce F; Pitkeathly D A
CS Medical Unit A, Southern General Hospital, Glasgow.
SO ANNALS OF THE RHEUMATIC DISEASES, **(1989 May)** 48 (5) 396-9.
Journal code: 62W. ISSN: 0003-4967.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198909
AB A placebo controlled, double blind study of aminohydroxypropylidene bisphosphonate (APD), given by monthly intravenous infusion, was conducted in 40 patients with rheumatoid arthritis. Biochemical markers of increased bone resorption, such as fasting urinary calcium/creatinine ratio and hydroxyproline/creatinine ratio, were suppressed significantly in the APD group to approximately 50% and 60% of the pretreatment level respectively, and serum calcium fell transiently after the first APD infusion. There was

no significant effect on disease activity in either the APD or placebo groups as judged by clinical (grip strength, morning stiffness, visual analogue score) or laboratory (haemoglobin, platelet count, erythrocyte sedimentation rate, C reactive protein) criteria. An exception was the articular index which improved to a similar degree in both groups, falling from (mean (SEM] 13.8 (1.8) to 7.2 (2.2) in the APD group and from 13.7 (1.9) to 6.8 (1.5) in the placebo group. Radiological progression occurred to a similar degree in both groups as assessed by the Sharp index (mean (SEM) 86 (13.1) v 95 (12.9)-APD group; 103 (15.1) v 110 (15.8)-placebo group), but there was no significant change in the Larsen index in either group (mean (SEM) 53 (4.2) v 57 (3.8)-APD; 62 (5.8) v 63 (5.6)-placebo). The lack of effect on radiological progression in the APD group indicates that focal erosive disease may either have progressed as the result of a non-osteoclast related mechanism, or that the intensity of bone resorption was too great to be inhibited by the doses of APD used.(ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Female; Human; Male
***Arthritis, Rheumatoid: DT, drug therapy**
Arthritis, Rheumatoid: ME, metabolism
Arthritis, Rheumatoid: RA, radiography
Calcium: UR, urine
Clinical Trials
Creatinine: UR, urine
***Diphosphonates: TU, therapeutic use**
Double-Blind Method
Hydroxyproline: UR, urine
Middle Age
Random Allocation

RN **40391-99-9 (amidronate)**; 51-35-4 (Hydroxyproline); 60-27-5 (Creatinine); 7440-70-2 (Calcium)

CN **0 (Diphosphonates)**

L158 ANSWER 27 OF 30 MEDLINE

AN 88311750 MEDLINE

DN 88311750

TI A clinical and biochemical assessment of etidronate disodium in patients with active rheumatoid arthritis.

AU Bird H A; Hill J; Sitton N G; Dixon J S; Wright V

CS Clinical Pharmacology Unit, Royal Bath Hospital, Harrogate, United Kingdom..

SO CLINICAL RHEUMATOLOGY, **(1988 Mar)** 7 (1) 91-4.
Journal code: DI6. ISSN: 0770-3198.

CY Belgium

DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 198812

AB Diphosphonates reduce the rate of bone turnover. They have additional pharmacological properties improving adjuvant arthritis in rats and lowering ESR in this condition. We have evaluated etidronate disodium, a diphosphonate commonly prescribed in the United Kingdom for Paget's disease in patients with rheumatoid arthritis. Apart from an early improvement in articular index, perhaps reflecting anti-inflammatory activity, no significant change occurred in clinical variables or in laboratory indices of 'secondline' action at a dose of 5 mg/kg/day.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
Arthritis, Rheumatoid: BL, blood
***Arthritis, Rheumatoid: DT, drug therapy**
Arthritis, Rheumatoid: PP, physiopathology
Blood Sedimentation
Bone and Bones: PP, physiopathology
Clinical Trials
Etidronate Disodium: AE, adverse effects

*Etidronate Disodium: TU, therapeutic use
Gastrointestinal Diseases: CI, chemically induced
Middle Age
Pain: CI, chemically induced
RN **7414-83-7 (Etidronate Disodium)**

L158 ANSWER 28 OF 30 MEDLINE
AN 87152757 MEDLINE
DN 87152757
TI Effect of (chloro-4-phenyl) thiomethylene bisphosphonic acid (SR 41319) on the autoimmune disease activity in MRL/l mice.
AU Barbier A; Planchenault C; Breliere J C
SO AGENTS AND ACTIONS, **(1986 Dec)** 19 (5-6) 311-2.
Journal code: 2XZ. ISSN: 0065-4299.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198706
AB MRL - lpr/lpr (MRL/l) mice spontaneously develop an autoimmune pathology including arthritic lesions. SR 41319, a bisphosphonate, having previously shown to be active in in vitro and in vivo models of arthritis, the aim of this study was to search for its possible effect on the pathology of the MRL/l mice. Results showed that SR 41319 reduced the severity of the disease in its early stages and increased mean life span. Further investigation would be necessary to define the effect of the drug during later stages when major changes in immune status occurred.
CT Check Tags: Animal
***Autoimmune Diseases: IM, immunology**
Autoimmune Diseases: PA, pathology
***Diphosphonates: PD, pharmacology**
***Lupus Erythematosus, Systemic: IM, immunology**
Lupus Erythematosus, Systemic: PA, pathology
Mice
Mice, Inbred Strains
*Phospholipases: AI, antagonists & inhibitors
*Phospholipases A: AI, antagonists & inhibitors
RN **96538-83-9 (SR 41319)**
CN EC 3.1.- (Phospholipases); EC 3.1.1.- (Phospholipases A); **0 (Diphosphonates)**

L158 ANSWER 29 OF 30 MEDLINE
AN 86268177 MEDLINE
DN 86268177
TI Immobilization hypercalcemia associated with Landry-Guillain-Barre syndrome. Successful therapy with combined calcitonin and etidronate.
AU Meythaler J M; Korkor A B; Nanda T; Kumar N A; Fallon M
SO ARCHIVES OF INTERNAL MEDICINE, **(1986 Aug)** 146 (8) 1567-71.
Journal code: 7FS. ISSN: 0003-9926.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 198610
AB Two patients with immobilization hypercalcemia associated with Landry-Guillain-Barre syndrome had marked hypercalciuria (890 and 1136 mg/d [22.2 and 28.3 mmol/d]) and radiologic evidence of generalized osteopenia. Parathyroid hormone levels were either low or normal by C-terminal radioimmunoassay. Subtotal parathyroidectomy was performed in the one patient, with no improvement in serum or urinary calcium levels. A bone biopsy specimen revealed decreased cellular activity in the first patient and increased bone resorption in the second patient. Treatment with intravenous saline, furosemide, oral phosphate supplementation, mithramycin, and calcitonin alone was ineffective in lowering serum or urinary calcium levels. However, when subcutaneous calcitonin combined with oral etidronate disodium was used, a reduction in the serum calcium

level was observed within two days of therapy. Within one week of the start of this combined therapy, the calcium level returned to normal and urinary calcium excretion was substantially reduced.

CT Check Tags: Case Report; Human; Male
Adult
Aged
Bone and Bones: PA, pathology
*Calcitonin: AD, administration & dosage
Calcitonin: TU, therapeutic use
Calcium: BL, blood
Drug Therapy, Combination
*Etidronate Disodium: AD, administration & dosage
Etidronate Disodium: TU, therapeutic use
Hypercalcemia: BL, blood
*Hypercalcemia: DT, drug therapy
Hypercalcemia: ET, etiology
Hypercalcemia: PA, pathology
*Immobilization
***Polyradiculoneuropathy: CO, complications**

RN **7414-83-7 (Etidronate Disodium)**; 7440-70-2 (Calcium); 9007-12-9 (Calcitonin)

L158 ANSWER 30 OF 30 MEDLINE
AN 83148390 MEDLINE
DN 83148390
TI [Results of radium 224 therapy in ankylosing spondylitis (Strumpell-Marie-Bechterew disease)].
Ergebnisse einer Radium 224-Therapie der ankylosierenden Spondylitis (M. Strumpell-Marie-Bechterew).
AU Knop J; Stritzke P; Heller M; Redeker S; Crone-Munzebrock W
SO ZEITSCHRIFT FUR RHEUMATOLOGIE, **(1982 Nov-Dec)** 41 (6) 272-5.
Journal code: Y0V. ISSN: 0301-6382.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA German
FS Priority Journals
EM 198306
AB After an average of 5 years following therapy with Ra224, the concentration of Tc99m methyl diphosphonate (MDP) in the region of the sacroiliac joints and lumbar spine was measured in 15 patients with ankylosing spondylitis. The findings were supplemented by those of clinical, pathological, and roentgenological examinations. The concentration of MDP was normal in the sacroiliac joints in almost all the patients, but was raised in the lumbar spine in two-thirds. This is to be interpreted as indicating enhanced bone turnover, the difference from that in healthy subjects being highly significant (p less than 1). Increased ossification of the lumbar spine could be demonstrated roentgenologically in two-thirds of the patients. Differential blood count, blood sedimentation rate, and electrophoresis remained unchanged after therapy. However, in 60% of patients the mobility of the spine was the same or even improved; 46% felt better after Ra224 treatment than before it.

CT Check Tags: Female; Human; Male
Adult
Diphosphonates: ME, metabolism
English Abstract
Lumbosacral Region
Middle Age
Ossification, Heterotopic: DI, diagnosis
*Radium: TU, therapeutic use
Spine: ME, metabolism
***Spondylitis, Ankylosing: RT, radiotherapy**

RN **1984-15-2 (methylene diphosphonate)**; 7440-14-4 (Radium)
CN **0 (Diphosphonates)**